LAW OFFICES

SHOOK, HARDY & BACON

COMPILATION OF ARTICLE SUMMARIES FROM ETS/IAQ REPORT

A Current Reference Document

Compilation 10
July–September 1994 • Issues 76-81

Collected From the Reports on Recent
ETS and IAQ Developments

SHB

— TABLE OF CONTENTS —

Please note: This document is not intended to be an encyclopedic summary of scientific literature relating to ETS. Rather, it only contains summaries and excerpts from those studies included in *Reports on Recent ETS and IAQ Developments.*

The summaries contained in this document are intended as a reference; the actual articles should be consulted for any purpose beyond a summary reference.

ENVIRONMENTAL TOBACCO SMOKE & INDOOR AIR QUALITY

ARTICLE SUMMARIES FROM ETS/IAQ REPORT

LUNG CANCER

[1] **de Wolff, F.A., "Risk of Lung Cancer Due to Passive Smoking Still Unproven," *Tijdschrift Voor Geneeskunde* (March 5): 503-506, 1994 [Issue 79, Item 28]**

In this article, the author analyzes EPA's scientific methodology used in its ETS Risk Assessment to determine whether the claim of 3,000 deaths per year due to lung cancer is based on adequate data. The article suggests that the ability to accurately measure ETS exposure is necessary in order to be able to study possible carcinogenic effects in humans and that this should be carried out without bias.

EXCERPTS:

"Since the early 80s, a considerable number of investigations have been carried out in which the possible effects of environmental tobacco smoke have been studied. This has lead [sic] to a series of publications announcing conflicting conclusions, culminating in the appearance, a few months ago, of a voluminous report by the American Environmental Protection Agency (EPA). Most important conclusion [sic] of this report was that passive smoking in the US alone caused 3000 deaths per year resulting from lung cancer. In children, environmental tobacco smoke was said to be the cause of increased risk of airway infections and asthma."

"The smoke to which the non-smoker is exposed is of an entirely different physical and chemical composition than the smoke to which the tobacco consumer himself is exposed. . . . The passive smoker is exposed to a lesser degree to the smoke exhaled by the active smoker. This smoke, in combination with the secondary stream smoke, forms the environmental tobacco smoke."

"The highly complex and variable composition of the smoke forms a problem in risk-evaluation for passive smoking."

"There are various ways of establishing the dosage of environmental smoke, in order to relate possible effects to such exposure. The simplest approach is the determination of the smoke components in the air, in or out of the breathing area of the persons to be studied. . . . The internal dosage can be determined by measurement of substances or metabolites characteristic of environmental smoke in blood, urine, or air exhaled by exposed persons."

"An oft-utilized biomarker for exposure to tobacco smoke which reasonably fulfills these conditions is cotinine."

"It is often forgotten that cotinine is not very specific as a biomarker."

"No laboratory method whatsoever fulfills all the criteria for the measurement of passive exposure of the human to tobacco smoke, and even the least inadequate method - determination of the nicotine metabolite cotinine in plasma - is not practicable in order to incontestably establish the assimilation of environmental tobacco smoke."

"Because reliable dosimetric data are lacking, it is impossible to directly connect a perceived effect, such as lung cancer, with exposure to environmental tobacco smoke."

"[A] rough estimate of exposure might be acceptable if the connection between exposure and effect were really clear. But the relative risks described are slight; they are of the magnitude 1.3. . . . This bias is probably caused by the fact that the investigators are so convinced of the harmful effects of active smoking that they are hard to put to express themselves in any other way than negatively with regard to smoking habits."

"In a number of publications, histopathologic data are entirely absent."

"One may ask oneself upon what grounds the EPA has decided to make such definitive statements, considering the uncertainties of a toxicologic and epidemiologic nature which have appeared in the investigation into the possible connection between passive smoking and lung cancer."

"The reader of the EPA report gets the uneasy feeling that a certain selectivity cannot be excluded. Scientific data are taken out of their larger context and utilized to show that passive smoking, just like active smoking, is harmful. This is a dangerous development against which the scientific community must actively defend itself."

"[A] 'causal' connection between environmental tobacco smoke and lung cancer is being postulated whereas there

does not yet exist a good system of measurement of exposure. . . . [P]riority will have to be placed upon the development of methods to unambiguously assess internal exposure to environmental tobacco smoke, in order to be able to study the possible carcinogenic effect of smoke to humans."

[2] **Letters to the Editor Regarding Gross, A.J., "Does Exposure to Second-Hand Smoke Increase Lung Cancer Risk?"** ***Chance: New Directions for Statistics and Computing*** **6(4): 11-14, 1994 [Issue 77, Item 33]**

A letter from Dorothy Rice and Stanton Glantz concerning the publication of articles on ETS and lung cancer by Alan Gross and Howard Rockette and a reply by the editors of *Chance* were recently published. *See* issue 74 of this Report, June 10, 1994, for the original articles. The letters appear as "Reaction to Environmental Smoke," *Chance* 7(1): 4, 1994.

Rice and Glantz criticize *Chance* for publishing articles that "make it appear that the question of whether passive smoking causes lung cancer remains controversial among the general scientific community." They also say that the Gross article does not present "an accurate and balanced review of the literature," and characterize it as presenting "results heavily biased in behalf of the sponsors of the work." Rice and Glantz question the quality of the review process at *Chance* and contend that the Gross article "will almost certainly be cited by the tobacco industry to support its position that ETS is not harmful because it was published in a prestigious journal."

In reply, the editors state that, in their opinion, "the evidence causally linking lung cancer to second-hand smoke is not so clear to preclude publishing alternative interpretations." They note that, while Gross' article may be "taken out of context," they judged presenting "different interpretations of the ETS evidence" to be "worth the risk."

[3] **Letters to the Editor Regarding Gross, A.J., "Does Exposure to Second-Hand Smoke Increase Lung Cancer Risk?"** ***Chance*** **6(4): 11-14, 1994 [Issue 80, Item 31]**

Three letters concerning an article by Alan J. Gross were recently published by the journal *Chance*. In the original article, Gross contended that the data on ETS exposure and lung cancer were inconclusive; in a companion article, Howard E. Rockette, a member of the Science Advisory Board committee that reviewed EPA's Risk Assessment on ETS, supported EPA's conclusion that ETS is a carcinogen. *See* issue 74 of this Report, June 10, 1994, for the original articles. Letters by Albert B. Lowenfels and Stephen M. Smith, and a reply by Gross to an earlier letter by Stanton Glantz and Dorothy Rice, appear at *Chance* 7(2): 4-5, 1994. *See* issue 77 of this Report, July 29, 1994, for the Glantz and Rice letter.

In his letter, Lowenfels proposes that it is "extremely unlikely" that an author "supported by the tobacco industry" would report a positive relationship for ETS and lung cancer. He suggests that Rockette's article "puts the problem in perspective," and concludes: "We can no longer take chances with the health of the public. Let's get this issue behind us."

Smith calls Gross' and Rockette's exchange of views "fascinating and alarming." He expresses criticism of Gross' approach, stating that "conventional statistical approaches . . . have served us very badly indeed" in assessing environmental questions. Smith calls for the "burden of proof" about claimed health effects of ETS to "be on the industry to show that there is *no* effect." He also suggests that the tobacco industry should fund clinical research "instead of paying its consultants to point out the flaws in existing studies."

In his letter, Gross states that the arguments advanced by Rice and Glantz are "clearly wrong," and says that "the letter's purpose -- to stifle scientific debate -- is pernicious." Gross says that, without free scientific exchange, "the advancement of science cannot continue, and a stagnation in science will occur." Finally, he claims that Glantz has never acknowledged that he was the founder of Californians (now Americans) for Nonsmokers' Rights. Gross suggests that Glantz has not done so because he believes himself to be on the "'right' (i.e., 'politically correct') side of the ETS issue." Gross concludes: "If Dr. Glantz's position is so clearly correct, one wonders why he fears publication of an opposing view."

[4] **LeVois, M.E., and Layard, M.W., "Inconsistency Between Workplace and Spousal Studies of Environmental Tobacco Smoke and Lung Cancer,"** ***Regulatory Toxicology and Pharmacology*** **19: 309-316, 1994 [Issue 76, Item 33]**

The authors of this article present analyses of the data on spousal smoking and lung cancer and on reported workplace exposures to ETS and lung cancer. They note that the two types of data support contradictory conclusions, and suggest that this difference invalidates the conclusions of the EPA Risk Assessment on ETS.

EXCERPTS:

"[T]here are problems with the EPA's risk determination. Its meta-analysis of U.S. studies omitted two studies which were published before the EPA document was released: Brownson et al. (1992) and Stockwell et al. (1992). Using the EPA's methods and assumptions, we have calculated a summary relative risk of 1.07 from a meta-analysis of 13 U.S. female spousal smoking studies, including these two recent studies. This relative risk, with 95% confidence interval of 0.95-1.21, is not statistically significant. Furthermore, there is highly significant inconsistency between the summary relative risks for six country-specific groups of female spousal smoking studies considered by the EPA. These relative risks are all either only weakly elevated or, in the case of China, below 1.0. In Section 2 we point out that a likely explanation for this geographic inconsistency is bias and confounding introduced by using spousal smoking as an exposure surrogate. In Section 3 we examine the epidemiologic data on workplace ETS exposure, which were ignored by the EPA but which overall exhibit no risk elevation. The inconsistency between the spousal and workplace studies supports the hypothesis that small risk elevations reported in some spousal studies are due to uncontrolled bias and confounding."

"A more likely explanation for the geographic inconsistency is that the reported associations are the product of uncontrolled bias and confounding linked with spousal smoking status and operating in varying degrees in different countries. Spousal smoking is a proxy, or indirect measure of actual ETS exposure, and its use introduces a host of concordant exposures, many of which are potential confounders of reported spousal smoking-lung cancer associations. Spouses share many important environmental and behavioral risk factors that are likely to confound a reported ETS-lung cancer association. For example, smokers and their spouses have been shown to have diets lower in fruits and vegetables, and higher in fat and alcohol consumption, than nonsmoking couples. The magnitude of dietary confounding is thought to be at least as large as the reported U.S. spousal smoking-lung cancer association. . . . None of the ETS-lung cancer epidemiologic studies adequately accounts for the effects of most of the known potential confounders."

"[T]he spousal smoking study design is generally agreed to be biased by the misclassification of some current and exsmokers as never-smokers. Because spouses of smokers are more likely to be smokers themselves than spouses of nonsmokers, denial of smoking is likely to upwardly bias lung cancer relative risks in spousal smoking studies. The EPA made some adjustment for smoking status misclassification, but it is doubtful whether the adjustment for the U.S. female studies was adequate, in the light of available information on misclassification rates."

"As part of its justification for concluding that ETS should be classified as a Group A carcinogen, the EPA claimed that the proportion of spousal smoking studies reporting a lung cancer risk elevation is improbably high and cannot be attributed to chance alone. . . . Given the large number of studies, all using the flawed spousal smoking study design, a statistical test of association based on the proportion of positive studies will with high probability detect the influence of bias and confounding inherent in that design; that is, such a test will likely be significant simply due to artifact."

"[A] comparison between the workplace ETS-lung cancer data and the spousal smoking data indicates that the workplace data are not consistent with even the weak risk elevations reported in some spousal smoking studies, and indeed the combined workplace studies exhibit no ETS-lung cancer association."

"To make this comparison, we performed, using the summarization method employed by the EPA, a meta-analysis of the results of 12 studies that have reported lung cancer relative risks for workplace exposure to ETS. . . . Of the 12 studies, 7 were conducted in the United States, 3 in Asia, and 2 in Europe. . . . The authors of two U.S. female studies, Brownson et al. (1992) and Stockwell et al. (1992), considered workplace ETS exposure and reported no significant increase in lung cancer risk, but did not present numerical results. . . . The summary relative risk for 12 of the 14 worldwide studies was 1.01, with 95% confidence interval (0.92, 1.11). The summary relative risk for 7 of the 9 U.S. studies was 0.98 with 95% confidence interval (0.98, 1.09). Although we could not include the Brownson et al. (1992) and Stockwell et al. (1992) studies in the meta-analyses, since they did not report relative risk estimates for workplace exposure, the authors' comments . . . indicate that including them would not change the conclusion that there is no epidemiologic evidence of an association between workplace ETS exposure and lung cancer."

"[N]onoccupational ETS exposure could not eliminate the effect of workplace exposure if a real association existed, so the combined results of the 12 studies, showing no lung cancer risk elevation, stand as evidence against the existence of a link between lung cancer risk and ETS exposure."

"The fact that, with the exception of China, summary relative risks from spousal smoking lung cancer studies are

higher than that from workplace ETS studies supports the arguments of Section 2 that the reported spousal smoking risk elevation is a consequence of bias and confounding factors that are introduced by the spousal smoking study design. Workplace studies would not be subject to bias and confounding due to spousal concordance, and this is a likely explanation for the inconsistency between workplace and spousal smoking findings."

"The fact that workplace studies produce a risk estimate that disagrees with the estimate derived from aggregated spousal smoking studies cannot be dismissed by making speculative assumptions about study design validity. The least that should be expected is that a diligent effort be made to evaluate the reasons for the discrepancy. Such an evaluation must seriously consider the possibility that it is the spousal smoking study design that is more severely flawed. As well as many other potential confounders, the spousal study design introduces socioeconomic status-mediated occupational risk factors. . . . The workplace ETS study design avoids problems of spousal concordance with respect to lung cancer risk factors and introduces fewer potential biases and confounders that are present in the spousal study design. Thus, workplace ETS-lung cancer data are probably less flawed than are the spousal smoking data."

"Since probable effects of bias and confounding have not been adequately accounted for in the spousal smoking-lung cancer epidemiologic studies, the EPA's conclusion that these studies support a causal inference is not justified."

"The aggregated workplace data indicate no ETS-lung cancer risk elevation, further undermining both a causal inference based on spousal smoking studies and the EPA's conclusions that ETS is a Group A carcinogen. The ETS-lung cancer epidemiologic data provide no scientific basis for government regulation of smoking in the workplace."

[5] **Pershagen, G., "Passive Smoking and Lung Cancer." In: *Epidemiology of Lung Cancer.* J.M. Samet (ed.). New York, Marcel Dekker, 109-130, 1994 [Issue 77, Item 34]**

In this review, the author claims that various lines of evidence support the carcinogenicity of ETS. However, he also states that "cancer induction is probably not the most significant effect of ETS from a public health point of view."

EXCERPTS:

"Although cancer induction is probably not the most significant effect of ETS from a public health point of view, there is no doubt that the potential for such effects has had a great impact on the attitudes towards passive smoking and constituted an important incentive for measures to restrict the exposure."

"This review focuses on the epidemiological evidence regarding passive smoking and lung cancer. Exposure to ETS is discussed initially, especially in relation to doses received by smokers. After summarizing the data on ETS and lung cancer, bias and methodological aspects of importance for the assessment of causal relationships are highlighted. Comparisons are also made of exposure-response relationships in passive smokers and smokers."

"It is necessary to consider various sources of bias and their implications in the assessment of the epidemiological evidence on passive smoking and lung cancer. This is particularly relevant in view of the weak associations observed, i.e., relative risks mostly ranging between 0.5 and 2. The assessment of bias should preferentially involve also its quantitative implications for the estimated associations."

"Probably the most important potential source of bias in the epidemiological studies on ETS and lung cancer is confounding by unreported active smoking."

"It seems unlikely that the effects of other confounding factors would exceed those of smoking."

"The evidence on ETS and lung cancer has been thoroughly reviewed by various groups. The conclusions reached are quite coherent in that environmental tobacco smoke can cause lung cancer. Subsequent evidence provides no reason to change the conclusions. For the quantitative assessment there is, however, a need for additional data on misreporting of smoking by lung cancer cases to enable a more detailed estimation of confounding and for more precise information on lifetime ETS exposure to reduce misclassification bias."

"Large segments of the population in many countries are exposed to ETS, which means that even small effects of this exposure may be of public health significance. Using biological markers, it has been estimated that the daily exposure to nicotine in passive smokers may correspond to a dose received from 0.1-1 cigarette in a smoker. The relative exposure for passive smokers in comparison with smokers varies substantially for different components in the smoke."

"More than 25 epidemiological studies have been published on passive smoking and lung cancer. The most common approach in the analysis has been to base the exposure classification on smoking habits of spouses.

Taking the studies together there is statistically significant increase in the lung cancer risk of about 20-30% in nonsmokers married to smokers. Higher risks in those married to heavy smokers were often observed, supporting a causal association."

"It is probable that a part of the increased risk related to smoking of spouses is explained by confounding by smoking. On the other hand, nondifferential misclassification of ETS exposure, resulting from crude exposure measures, will give rise to an underestimation of the true risks. The available empirical data suggest that bias cannot explain the observed association between ETS exposure and lung cancer. An overall assessment taking into consideration the presence of carcinogens in ETS, exposure estimates in passive smokers, exposure-response relationships in smokers, and the epidemiological evidence on lung cancer in passive smokers indicates that ETS is of carcinogenic importance."

[6] Letters to the Editor Regarding Rennie, D., "Smoke and Letters," *Journal of the American Medical Association* 270(14): 1742-1743, 1993 [Issue 76, Item 34]

An additional exchange of correspondence has been published concerning Drummond Rennie's editorial on the role of the editor in evaluating letters for publication. *See* issue 58 of this Report, October 22, 1993. A letter by Steven Parrish, of the Philip Morris Company, and a reply by Rennie were published at *Journal of the American Medical Association* 271(20): 1575, 1994.

Parrish's letter states that Rennie's editorial exhibited "lack of balance, selective use of data, and the very type of bias that Rennie accuses the tobacco industry of practicing." He also suggests that Rennie's questioning of the veracity of authors affiliated with the tobacco industry "has no place in a medical journal." Parrish writes that Rennie "is selective in his choice of ammunition" in the editorial, noting that, while Rennie mentioned the *AFCO* case, he failed to mention that the case had been reversed on appeal, and that the *Burswood Casino* case ruling cautioned against selective interpretation of data. Parrish closes his letter by calling on *JAMA* to "rigorously apply balance and fairness to all subjects, no matter how controversial they might be." The *AFCO* and *Burswood* cases were decided in Australia.

In his reply, Rennie claims that he did not question the veracity of those authors writing the critical letters that prompted his editorial. He claims that Parrish's description of the *AFCO* appeal is "simply untrue," stating that while the higher court had not reexamined the scientific data, it nevertheless affirmed the lower court's conclusion. Rennie also suggests that the reference to *Burswood Casino* was irrelevant, as that case dealt with adult respiratory illness or impairment, rather than cancer. Finally, Rennie implies that Parrish's letter is a case of "misdirection by the tobacco industry," and suggests that the letter and his editorial be compared for "lack of balance, selective use of data, and bias."

[7] Smith, G.D., Strobele, S.A., and Egger, M., "Smoking and Health Promotion in Nazi Germany," *Journal of Epidemiology and Community Health* 48: 220-223, 1994 [Issue 78, Item 26]

Although this historical review focuses on German efforts to reduce the prevalence of active smoking, the authors mention an early German study that apparently proposed a link between lung cancer in nonsmoking women and their husbands' smoking.

EXCERPTS:

"While accusations about the health damaging effects of tobacco stretch back over the centuries, a particularly strong tradition of scientific investigation emerged in Weimar Germany and was developed during the Nazi period. Take, for example, the case of smoking and lung cancer. While there were earlier anecdotal reports, from Germany and elsewhere, commenting on a possible link, the 1928 study by Schonherr in Chemnitz is considered seminal in focussing on the smoking habits of a series of lung cancer patients. The small group of women in this series apparently did not smoke, but, Schonherr concluded, their cancers could have been caused by inhalation of their husbands' smoke."

[8] Vandenbroucke, J.P., "Health Risks from Passive Smoking: Opposite Results or Opposite Opinions?" *Ned. Tijdschr. Geneeskd.* 139(10): 507-508, 1994 [Issue 80, Item 32]

The author of this commentary proposes that debate about the claimed health effects of ETS exposure remains a possibility. He also discusses the difficulty of making decisions from a policy-making versus a scientific viewpoint.

EXCERPTS:

"By some, the potential carcinogenicity of passive smoking is used as yet another reason for denouncing the use of tobacco, especially cigarettes. In view of the fact that the scientific reasoning is not airtight -- even the epidemiologists who have contributed to the study of the harmful effects of active smoking, such as Mantel

mentioned above, have their doubts -- there exists the danger that those who are leading the antismoking campaign will be shown to be in the wrong or will lose credibility on this point."

"Many are having difficulty in distinguishing between the specific role of the scientist and that of the policy-maker. A policy-maker has the duty to make decisions, even if uncertainty prevails. A scientist, in contrast, has the job of examining hypotheses, whether these fall under a certain policy or not. In other words, scientists may not wear the hat of a policy-maker and policy-makers may not wear the hat of a scientist."

"Concerning passive smoking, debate remains possible; reputable scientists come to opposite conclusions. This should neither surprise us nor scandalize us. Uncertainty prevails on the front lines of scientific progress. No one can predict what the future will reveal as the truth or who will turn out to have been right. Who ultimately turns out to have been right is in fact unimportant; ultimately, we all share in the same prize, the truth based on knowledge. It is even possible that the future 'I-told-you-so's' might not have had the best arguments to begin with."

"At this moment, policy-makers must decide whether the current data on passive smoking constitute sufficient grounds for taking action. The scientific debate about passive smoking, however, should not hold them back from enacting much stronger measures to discourage active smoking."

CARDIOVASCULAR ISSUES

[1] **Brown, R.E., Nahser, P.J., Rossen, J.D., Winniford, M.D., "Vasoconstriction of Coronary Stenoses from Exposure to Environmental Tobacco Smoke," *Journal of the American College of Cardiology* (Special Issue): 107A, 1994 [Issue 81, Item 18]**

In this meeting abstract, the authors report that, in six patients exposed to high concentrations of ETS in a chamber, the diameter of coronary stenoses (constrictions) decreased. They conclude that this "may contribute to the adverse cardiovascular effects" claimed to be due to ETS.

EXCERPTS:

"We have previously reported that ETS exposure causes modest constriction of non-stenotic coronary segments. The present study was performed to assess the effect of ETS exposure in stenotic coronary arterial segments. We measured the coronary artery diameter at the site of a stenosis (>50% diameter reduction) in 6 patients . . . before and after exposure to ETS. Sidestream tobacco smoke was vented into a chamber placed over the patient's head, maintaining an average carbon monoxide level of 30 ppm. In 3 control subjects, room air without tobacco smoke was used. Quantitative coronary angiography was performed at baseline and after 15 minutes of ETS or room air exposure. Blood pressure, heart rate and serum carboxyhemoglobin (CO) were recorded at each point."

"Minimum coronary stenosis diameter fell 13% from 1.6±0.4 mm at baseline to 1.4±0.4 mm after ETS. This corresponds to a 24% reduction in minimum cross-sectional area of a circular stenosis. After exposure to ETS, CO increased from 0.63 to 0.83 ppm, while HR and BP were unchanged. In the 3 control subjects, there was no significant change in coronary diameter, HR or BP."

"Exposure to environmental tobacco smoke causes vasoconstriction at the site of coronary stenoses. This may contribute to the adverse cardiovascular effects of passive smoke exposure."

[2] **Letters to the Editor Regarding Glantz, S.A., and Parmley, W.W., "Passive Smoking and Heart Disease: Epidemiology, Physiology and Biochemistry," *Circulation* 83: 1-12, 1991 [Issue 79, Item 29]**

The *Journal of Clinical Epidemiology* recently published two letters concerning the 1991 Glantz and Parmley article, which claimed that 53,000 heart disease deaths could be attributed to environmental tobacco smoke exposure. A letter by Peter N. Lee and a reply by Glantz and Parmley appear at *Journal of Clinical Epidemiology* 47: 303-304, 1994.

In his letter, Mr. Lee takes objection to an attack on his credibility based on his previous work on behalf of the tobacco industry. "It is the data that are important, not who presents them," Mr. Lee states. "It does not concern me that Glantz is an antismoking activist and a founder of Americans for Nonsmokers' Rights," he continues. "What does concern me is that the original paper has errors in it that, even when pointed out, are not accepted." In his conclusion, Mr. Lee refers to his latest publication claiming that the conclusions of EPA Risk Assessment on ETS are unsoundly based, and notes that EPA did not concur with Glantz and Parmley's claims about ETS and heart disease.

In their reply, Glantz and Parmley say that they "are frankly puzzled by Mr. Lee's continued insistence" that

an analysis in their paper "is wrong." They continue by saying, "Mr. Lee ignores the fact that we reviewed 13 studies on passive smoking and heart disease . . . and that, except for Mr. Lee's study, they show a consistent elevation in risk of heart disease death associated with exposure to ETS." They also refer to the ETS risk assessment, stating that Mr. Lee's comments are "misleading" because it is "a report on '*Respiratory* health effects of passive smoking, lung cancer and other disorders,' . . . not heart disease." Glantz and Parmley conclude that although the "EPA has not taken an official position on passive smoking and heart disease, the American Heart Association has."

[3] **Howard, G., Burke, G.L., Szklo, M., Tell, G.S., Eckfeldt, J., Evans, G., and Heiss, G., "Active and Passive Smoking Are Associated with Increased Carotid Wall Thickness: The Atherosclerosis Risk in Communities Study," *Archives of Internal Medicine* 154: 1277-1282, 1994 [Issue 78, Item 27]**

Carotid wall thickness, as an index of atherosclerosis, was measured in smokers, exsmokers, reportedly ETS exposed nonsmokers, and reportedly non-exposed nonsmokers. The authors claim that their data support an association between ETS exposure and carotid wall thickness, and that ETS exposure may be an atherosclerosis risk factor.

EXCERPTS:

"This article describes the effects of active and passive smoking on carotid artery intimal-medial thickness (IMT) in a population-based sample of middle-aged adults and the dose-response relationships both of IMT with pack-years of smoking among current and past smokers and of IMT with hours of exposure to ETS among nonsmokers."

"Mean IMT was higher in ETS smokers than in nonsmokers. It was highest in current and past smokers. . . . The differences between the mean IMT of nonsmokers and that of ETS smokers was similar in magnitude to that of a 1-year age difference, whereas the difference in IMT between current smokers and nonsmokers was similar to that of a 7-year age difference."

"The relationship between the reported number of hours of ETS exposure and IMT was assessed among those participants in the ETS exposure group. The number of hours of ETS exposure was significantly associated with IMT in men. For the 885 men with ETS exposure, after controlling for age and race, there was an increase in IMT of 0.00792 mm per 10 hours of weekly ETS exposure, a relationship that proved statistically significant. Despite a larger sample of ETS women (n = 2340), the increase in IMT per 10 hours of ETS exposure was only 0.0011 mm, a difference that proved statistically insignificant."

"These data confirm the findings of previous investigations showing that active smokers have thicker carotid artery walls than nonsmokers do. We also observed increased IMT in nonsmokers exposed to ETS than in nonexposed nonsmokers."

"We noted that IMT in ETS smokers falls between that of never smokers with no ETS exposure and that of past smokers (with current smokers having the highest IMT). . . . The higher IMT percentiles likely represent established atherosclerotic plaques. Thus, the largest differences between smoking groups were observed in those participants most likely to have manifest atherosclerosis."

"These analyses show that ETS smokers have, on average, IMT values 0.017 mm greater than those of nonsmokers. In the entire ARIC population, the cross-sectional relationship between age and IMT showed an estimated increase of 0.011 mm per year of age. This difference between the ETS smoking and nonsmoking groups (0.017 mm) is equivalent to the difference associated with approximately 1.5 years of aging and could potentially be explained by differences in lifestyle factors other than smoking between these groups. However, adjustment for lifestyle factors and major cardiovascular disease risk factors did not explain the observed difference between nonsmokers and ETS smokers."

"Importantly, the nonsmokers who reported no current exposure to ETS could well have been exposed to ETS in the past. Hence, among those categorized as nonsmokers there is likely a subgroup regularly exposed to ETS in the past. Significant differences were observed despite this misclassification that would reduce the observed ETS-IMT relationship. However, on average, those who reported current exposure to ETS were likely to have higher ETS exposure than those who reported no such current exposure."

"We estimated a much larger increase in IMT with increasing ETS exposure for men than for women. Even with the smaller sample size for men, statistical significance was reached, whereas in women there was no significant relationship. The reason for this difference is not clear. It is not explained by differences in the distribution of the number of hours of ETS exposure, which was similar for men and women. While the gender difference may result from differential misreporting of ETS exposure

(when the participant was actually a current smoker), there was no evidence of a gender difference in misclassification in a younger population. It is possible that men have more 'intense' ETS exposure (i.e., a more dense ETS environment) than women. Household exposures to ETS have been shown to be less than exposure levels observed in the workplace, and men may receive a larger proportion of their exposure in the workplace. The effect of increasing hours of ETS exposure was not small. For 40 hours of ETS exposure (equivalent to being in a smoking work environment), there is an estimated increase of 0.0317 mm in average IMT. This difference in IMT is equivalent to a more than 3-year age difference."

"In the ARIC Study cohort, the increase in mean carotid IMT associated with passive smoking represents a difference of 2.4% from the IMT of nonsmokers. Although differences in IMT of this magnitude are ostensibly unimpressive and would contribute only slightly to the risk of cardiovascular disease for an individual, the potential public health impact is not trivial, as it depends on both the magnitude of the estimated association and the frequency of occurrence of exposure at issue in the population. In the ARIC Study population, exposure to ETS among nonsmokers was 65%, which represents the proportion of individuals at risk of end-organ damage attributable to exposure to ETS. Relative to nonsmokers, ETS smokers had an IMT 0.017 mm greater (after adjustment for age, race, and gender), a difference equivalent to that associated with an increase of 1.5 years of chronologic age, or 7 mm Hg of systolic blood pressure, or 0.70 mmol/L (27 mg/dL) of total plasma cholesterol in this population."

"At age 55 years (arbitrarily chosen as the middle age of the population), the magnitude of the association between passive smoking and IMT corresponded to 23% of that observed for active smoking, the latter being one of the strongest and most consistently replicated associations between IMT and any physical, behavioral, or environmental exposure. The graded, monotonically increasing dose-response relationship observed between tobacco smoke and IMT adds to the biologic plausibility of the observed association between ETS and IMT. The association is detectable at the modest level observed for the exposure to ETS to the marked association seen with active smoking."

[4] McPhillips, J.B., Eaton, C.B., Gans, K.M., Derby, C.A., Lasater, T.M., McKenney, J.L., and Carleton, R.A., "Dietary Differences in Smokers and Nonsmokers from Two Southeastern New England Communities," *Journal of the American Dietary Association* 94: 287-292, 1994 [Issue 80, Item 33]

Although this article does not mention ETS exposure, its data on dietary differences between smokers and nonsmokers support the contention that diet may be a potential confounder in studies of spousal smoking and chronic disease. The authors report decreased consumption of fiber and vitamins in smoking women, and an increased consumption of fatty foods and alcohol in smoking men.

EXCERPTS:

"Previous studies based on 24-hour dietary recall data have shown that smokers tend to consume less healthful diets than nonsmokers. We tested this hypothesis using data from food frequency questionnaires (FFQs) in a group of men and women."

"Characteristics of smokers and nonsmokers were compared using data collected from a cross-sectional household health survey."

"Adults aged 18 through 64 years from two communities in southeastern New England were randomly selected for the study and interviewed in their homes by trained personnel. The interview included questions on demographic and behavioral characteristics. Height, weight, blood pressure, and serum lipids were measured using standard protocols. The Willett FFQ was completed by 1,608 of 2,531 eligible respondents who made up our study sample."

"Smokers reported higher total energy consumption than nonsmokers, although the difference was greater among men. . . . Smokers consumed more total and saturated fat than their nonsmoking counterparts, even after adjusting for age and energy intake from food. . . . Men who smoked reported consuming nearly twice as much alcohol as men who did not smoke; the difference by smoking status in women was much smaller."

"Women who smoked had lower intake of vitamins A and C, folate, and iron compared with women who did not smoke. . . . Men who smoked also consumed less of these nutrients than men who did not smoke, but the differences were smaller."

"Both men and women who smoked consumed more cholesterol and caffeine and less dietary fiber than nonsmokers."

"Smokers and nonsmokers differed with respect to consumption of food groups. In general, smokers consumed fewer servings of fruit, vegetables, and fish and poultry and more servings of processed meats, snack foods, and fats and oils."

"Multivariate adjustment for age, per capita income, regular exercise, marital status, and working status slightly reduced the strength but not the direction of associations between dietary components and smoking status. After adjusting for these confounders, smoking remained significantly associated with several diet variables including total fat, energy-adjusted fat, and percent of energy from fat, alcohol, caffeine, vitamin A, and folate."

"[M]ost studies show that smokers consume significantly more total or saturated fat, more energy, more alcohol, more caffeine or coffee, less dietary fiber, fewer servings of fruits and vegetables, less vitamin A, less vitamin C, and less folate than nonsmokers. In our study, we found that smokers consumed more total and saturated fat than nonsmokers. . . . We also found that smokers, especially men, consumed more energy than nonsmokers. However, this difference can be attributed to increased alcohol consumption among male smokers. . . . We were not surprised to find that women who smoked consumed significantly less vitamin A, vitamin C, dietary fiber, and folate than nonsmoking women because these nutrients are concentrated in fruits and vegetables, which were consumed less frequently by women who smoked."

"The lack of significant associations between diet variables and smoking in men is unlikely to be attributable to inadequate sample size because the magnitude of the differences in intake by smoking status was generally much smaller in men than in women."

"Our study suggests that smokers, especially women, may be at increased risk of disease morbidity and mortality because their diets are less healthful than those of women who do not smoke."

[5] **Sasajima, T., Kubo, Y., Izumi, Y., Inaba, M., and Goh, K., "Plantar or Dorsalis Pedis Artery Bypass in Buerger's Disease,"** ***Annals of Vascular Surgery*** **8: 248-257, 1994 [Issue 78, Item 28]**

While this article deals with the surgical treatment of thromboangiitis obliterans (Buerger's disease), the authors mention that ETS exposure may be considered as a clinical criterion in the diagnosis and treatment of this condition.

EXCERPTS:

"The peripheral type of Buerger's disease is unresponsive to conservative therapy when accompanied by multisegmental occlusion at the level of the ankle. Between November 1983 and April 1993, we performed 15 bypasses below the ankle for this type of thromboangiitis obliterans [TAO] in 13 patients (mean age 45.7 years), including four females. . . . Eleven patients were heavy smokers, two were passive smokers, and six had a history of sympathectomy. . . . Because patients with thromboangiitis obliterans are relatively young and active, early healing of ulcers and restoration of normal limb function are important objectives in their treatment. Bypass to the foot arteries can provide an excellent outcome, although special techniques and postoperative cessation of smoking are essential for success."

"Although the guidelines used to diagnose TAO are widely accepted in Japan, Shionoya described the following clinical criteria that do not include arteriographic findings for the diagnosis of TAO: (1) smoking history, (2) onset before age 50 years, (3) infrapopliteal arterial occlusive lesions, (4) either upper limb involvement or phlebitis migrans, and (5) absence of atherosclerotic risk factors other than smoking. However, the problem is how many criteria must be met to make a definite diagnosis of TAO. Our series included three patients with onset after age 50 years; one of them was 63 years old at the time of surgery, and the other two were female nonsmokers. The former satisfied all of the criteria except age of onset and the latter had a clear history of passive smoking, and the arteriograms of all three patients showed typical findings of TAO and the absence of arteriosclerotic lesions. To avoid overestimation of equivocal cases, we believe at least four of the five clinical criteria should be met, whereas Shionoya and Ishibashi et al. reported that TAO may affect men in their fifties and an outbreak of TAO in nonsmokers who are continually exposed to environmental tobacco smoke is also possible. Although the influence of passive smoking on patients with TAO remains controversial, there was more exposure to second-hand smoke in the home and workplace of female TAO patients who were nonsmokers compared with nonsmoking control subjects."

"After surgery all of our patients were given anticoagulant and antiplatelet drugs for 2 years, because vein graft stenosis frequently occurs within 2 years of surgery. However, the most important part of postoperative surveillance is to check for smoking, including passive smoking, because disease progression is closely related to smoking after surgery."

[6] **Wells, A.J., "Passive Smoking as a Cause of Heart Disease," *Journal of the American College of Cardiology* 24: 546-554, 1994 [Issue 78, Item 29]**

In this paper, A. Judson Wells, author of a 1988 paper estimating mortality due to ETS exposure, claims to calculate, using the methodology applied in the EPA Risk Assessment on ETS, that 62,000 ischemic heart disease deaths were associated with ETS exposure in the United States in 1985.

EXCERPTS:

"The present report reviews briefly the principal evidence connecting passive smoking with ischemic heart disease, including the most recent data. In addition, steps will be outlined that practicing physicians can take to protect their patients from environmental tobacco smoke exposure."

"Logically . . . one would expect environmental tobacco smoke exposure to result in heart disease but at a level lower than that from active smoking."

"There is one important difference between lung cancer and heart disease insofar as passive smoking is concerned. With lung cancer, the potentially fatal health effect results only from long-term exposure, perhaps _ 20 years, whereas with heart disease, the potentially fatal effects are not only long-term and chronic but short-term and acute as well."

"The acute effects of passive smoking on the cardiovascular system can occur from exposures of 20 min to 8 h. They are covered in detail by Glantz and Parmley. Suffice it to say here that these effects consist of 1) a decrease in platelet sensitivity that leads to greater platelet aggregation and increased risk of coronary thrombosis, and 2) an increase in oxygen demand by the heart at a time when oxygen supply is decreased and the heart's ability to process oxygen is also decreased."

"The other acute effect that environmental tobacco smoke has on the heart is a complex of effects driven largely by the carbon monoxide in the smoke."

"In the previous discussion on platelets it was stated that short-term exposure to environmental tobacco smoke results in increased endothelial cell carcasses in the blood. This indicates damage to the arterial endothelium, which is thought to be the initiating step in the development of atherosclerotic plaques."

"Environmental tobacco smoke also appears to have an effect on cholesterol in nonsmokers."

"In summary, as with active smoking, there is ample biologic evidence, including human evidence, that exposure to typical levels of environmental tobacco smoke can cause a buildup of arterial plaque and thus lead to heart attacks. Also there are acute effects related to the nicotine and carbon monoxide in environmental tobacco smoke that may be important mechanisms through which environmental tobacco smoke causes adverse heart effects."

"The available epidemiology associating passive smoking with heart disease is displayed in Table I. With 12 studies and 3,131 cases, it is almost as extensive as that associating passive smoking with lung cancer (30 studies and 3,083 cases). There is no heart study of the quality of the large Fontham et al. study on lung cancer, which was designed specifically for passive smoking and where data from five U.S. centers were combined. In that study both patients and control subjects provided serum samples for cotinine assay to eliminate smoker misclassification effects. . . . Another aspect that some investigators would regard as a strength is that the proportion of studies that are prospective (vs. case control) is much higher here (7 of 12) than in the lung cancer studies (4 of 30)."

"From the epidemiology, one can conclude that there appears to be a 20% to 70% increase in ischemic heart disease risk that is associated with exposure to spousal or household environmental tobacco smoke and that this increase in risk is not explained by misclassification of smokers as nonsmokers or by the other heart risk factors."

"Three risk assessments of ischemic heart deaths in the United States from passive smoking have so far been made. They are Wells, 32,000 deaths/year; Glantz and Parmley, 37,000 deaths/year (this is the Wells estimate when fully corrected for background environmental tobacco smoke); and Steenland who used a somewhat different procedure to arrive at 35,000 to 40,000 deaths/year. all three of these assessments were based on estimates of never-smoker heart death rates and the estimated population of never and ex-smokers. . . . In the recent EPA report on lung cancer and other respiratory diseases, a different methodology was used based on total lung cancer deaths, including those of smokers. This methodology will be applied here."

"In our heart case, we will start with the known total ischemic heart disease deaths for 1985, namely, 251,000 for women and 285,800 for men. . . . [W]e will assume that never-smoking men and women both have corrected passive smoking ischemic heart disease relative risks of 1.22 for the preferred case and 1.79."

"There are two other key variables that affect the risk assessment: 1) the ischemic heart disease relative risk for ever smokers relative to all never smokers, which we assume to be 1.7 for both genders; and 2) Z, the ratio of environmental tobacco smoke exposure from spousal smoking plus other environmental tobacco smoke exposures to exposure from other sources alone. . . . The EPA, in their lung cancer report, used Z_f for (women) = 1.75 based on five U.S. studies. We have chose a more conservative value of Z_f = 2.6 based on the median value for cotinine for the never-smoking women in the Fontham et al. study, which is the largest U.S. passive smoking/lung cancer study based on five population centers largely in the southern part of the United States, where most of the U.S. studies on heart disease and passive smoking are based. . . . [W]e have assumed Z_m (for men) = 2.6 X (1.27/1.55) = 2.1."

"Other important variables, which are the same for heart disease estimates and lung cancer estimates, are taken directly from the EPA report, namely, U.S. population ≥35 years old, 58 million women and 48 million men; ever-smoking prevalence of 44.3% for women and 72.8% for men; never-smoker spousal passive smoking exposure, 60% for women and 24% for men; ≥5-year ex-smoker population 8.7 million women and 15.0 million men; and the fraction of these ex-smokers exposed to spousal smoking, 77% for women and 41% for men."

"The preferred case, where the passive relative risk . . . is 1.22, the active smoking risk . . . is 1.7, the Z ratio for women . . . is 2.6, and that for men . . . is 2.1, yields an estimated total number of passive smoking ischemic heart disease deaths in the United States of 62,000 for 1985. The calculated deaths when data from tiers 1 and 2 only are included are 183,000. The estimated numbers of deaths are very sensitive."

"The estimated annual deaths . . . are considerably higher than the 32,000 to 40,000 noted in earlier studies. One reason is that the never-smoker death rates that we derive from the known total ischemic heart disease deaths in 1985 are higher than the never-smoker death rates assumed in the earlier risk assessments. Another reason is their use of Z = 3.0 based on early work in England whereas we have used the lower U.S. values."

"The percents for each category of the 536,800 total U.S. ischemic heart disease deaths are 4.5% for exposure to spousal tobacco smoke, 7.0% for exposure to background tobacco smoke, 34.5% for ever smoking and 54.0% for nontobacco causes. Thus, environmental tobacco smoke is estimated to cause (4.5 + 7.0)/34.5 = 33% as many cardiac deaths as those caused by active smoking."

"To summarize, on the basis of the rather thorough methods of the EPA to calculate deaths from passive smoking, the cardiac deaths so calculated are 40% to 100% higher than those calculated by earlier methods. What is thought to be the best estimate . . . indicates 62,000 ischemic heart disease deaths in the United States in 1985 caused by passive smoking. It is also possible, if more information about potential confounders can be obtained, that the toll is even higher."

"The major uncertainty in the ischemic heart disease death estimates and in whether or not a passive smoking effect exists arises because of the many other factors that might cause cardiac disease and death and might confound the passive smoking effect. Supporting evidence for an effect is the strong evidence of biologic plausibility, and, as adjustments are made for more cardiac risk factors, the passive smoking relative risks tend to increase. . . . Deaths calculated using the extremes of the 95% confidence interval values for the relative risk of 1.22 for the preferred case . . . indicate a range of 26,700 to 98,400 deaths/year."

"Ischemic heart disease appears to be by far the major mortality risk from passive smoking. There are both short- and long-term cardiovascular effects from passive smoking. Practicing physicians would do well to warn their at-risk heart patients to avoid smoky rooms. Such patients and the public in general should seek work where no-smoking rules apply; they should avoid riding in automobiles when others are smoking; and, if their spouses smoke, it should be suggested that they smoke outside the home."

[7] **Woodward, M., Bolton-Smith, C., and Tunstall-Pedoe, H., "Deficient Health Knowledge, Diet, and Other Lifestyles in Smokers: Is a Multifactorial Approach Required,"** ***Preventive Medicine*** **23: 354-361, 1994 [Issue 79, Item 30]**

The Scottish Heart Health Study randomly selected middle-aged men and women to compare health knowledge, behavior and lifestyles of 4,896 smokers and 4,595 nonsmokers. The authors report that smokers have poorer dietary knowledge and generally more "unhealthy" lifestyles than do nonsmokers. Although ETS is not mentioned, the data in this study suggest that lifestyle factors (such as diet) may be potential confounding factors in epidemiologic studies using spousal smoking as a surrogate for ETS exposure.

EXCERPTS:

"Data from the Scottish Heart Health Study, a random cross-sectional sample of middle-aged men and women, are used to compare health knowledge, behavior, and lifestyles between 4896 smokers and 4595 nonsmokers."

"Smokers are found to have poorer dietary knowledge than nonsmokers, although both groups are well-informed on some aspects of diet. Knowledge of personal risk modifiers for coronary heart disease and recent intention to improve lifestyle are both worse among smokers. Smokers have lower intakes of the antioxidant vitamins and fiber, but higher intakes of dietary cholesterol and alcohol than nonsmokers. They also tend to have higher salt intake and eat a greater proportion of saturated fat, butter, or hard margarine, and full-fat milk. High-density lipoprotein cholesterol levels are lower, but triglycerides, fibrinogen, and, for women only, total serum cholesterol levels are higher among smokers. On the other hand, body mass index and diastolic blood pressure are lower among smokers."

"In addition to advice to give up smoking, smokers should be counseled to improve their diet. The positive message to eat more fresh fruit and vegetables would be particularly helpful."

RESPIRATORY DISEASES AND CONDITIONS -- ADULTS

[1] Dayal, H.H., Khuder, S., Sharrar, R., and Trieff, N., "Passive Smoking in Obstructive Respiratory Diseases in an Industrialized Urban Population," *Environmental Research* 65: 161-171, 1994 [Issue 76, Item 35]

Based on a study of residents of several Philadelphia neighborhoods, the authors claim to show a statistically significant increased risk of obstructive pulmonary disease associated with the smoking of more than one pack per day in the home. They suggest that home exposures to ETS are more important than are exposures to ETS in workplaces or public places.

EXCERPTS:

"We wish to examine the association of obstructive respiratory disease with tobacco smoke in the residential environment, independent of active smoking, ambient air pollution, and some other sources of residential air pollution. A probability sample survey of nine neighborhoods in Philadelphia conducted in 1985-1986 provided an opportunity to examine this relationship."

"Analyses presented in this paper are based on information in the survey of approximately 4200 individuals regarding age, gender, active smoking, passive smoking, heating- and cooking-related measures of indoor air pollution, neighborhood of residence and whether the individual had a diagnosis of asthma, emphysema, or chronic bronchitis."

"Table 2 gives the distribution of passive smoking among people in the total sample with and without obstructive respiratory disease. The distribution in the two groups was significantly different. The prevalence varied according to the level of passive smoking in a dose-response fashion, with the group with exposure equivalent to greater than one pack per day having 40% higher prevalence than the one having no exposure to environmental tobacco smoke."

"[P]assive smoking was a significant factor in obstructive respiratory disease only for those people who themselves have never smoked."

"The passive smoking exposure at greater than one pack per day had a significantly elevated odds ratio of 1.86, and the 95% confidence interval did not include the null value of 1. The distribution of the passive smoking exposure in cases and controls combined in the >1 pack/day category was as follows: more than 1 but up to 2 packs/day, 68%; more than 2 but up to three packs/day, 19%; and more than 3 packs/day, 13%. The estimated odds ratio of 1.86 reflects the relative odds collectively for all subjects placed in the >1 pack/day category; the odds for those at the higher end of the category would be higher. Passive smoking exposures at lower level (<1 pack/day) did not confer a significant risk according to these data. Also, the method of heating and cooking as a source of indoor environmental pollution did not seem to have any effect on the risk of obstructive respiratory disease after one adjusted for tobacco smoke in the indoor environment."

"Most current and proposed policy initiatives in reducing exposure to ETS have restricted smoking in public places. However, a review of the literature reveals that almost all the evidence about the harmful effects of ETS has come from residential settings. The present study suggests that a smoker may be subjecting the nonsmoking members of the household to an almost two-fold risk of obstructive respiratory diseases over and above whatever risks are accorded by ambient air pollution in an urban environment."

"The present study has several limitations which may mediate their possible influence on the inferences. Fist,

2046343768

the passive smoking was characterized by information from a questionnaire as opposed to obtaining direct estimates from a biological marker or from air sampling measurements. It is generally recognized that the accurate determination of exposure to ETS is notoriously difficult. While it is possible to use a marker such as saliva or urinary cotinine (a nicotine metabolite) concentration as a determinant of ETS exposure in nonsmoking persons, such measures only calibrate exposures in the immediate past."

"The measure of passive smoking in the present study refers to the level of tobacco smoke in the home environment at the time of the interview. It is not possible, therefore, to construct a measure of lifetime ETS exposure."

"The present study did not take into account a number of factors that might possibly have an effect on the risk of obstructive respiratory disease, for instance, malnutrition and genetic predisposition. There is also a possibility, albeit remote, of a differential bias of unknown magnitude due to the fact that the ETS exposure outside the home environment did not factor into the calculation nor was any adjustment made for the portion of smoking done by a household member outside the house."

"The unique contribution of this study is that it establishes passive smoking as a significant risk factor for obstructive lung diseases for nonsmokers, controlling for the effect of ambient air pollution on such risk. This could be accomplished because we had a sufficiently large sample in each neighborhood and matching by neighborhood effectively controlled for quality of ambient air. However, the elevated risk is significant only at the level of greater than one pack per day of tobacco smoke in the household environment. This may be indicative of a real threshold effect or may be due to the limitations of the study as discussed above."

[2] **Ostro, B.D., Lipsett, M.J., Mann, J.K., Wiener, M.B., and Selner, J., "Indoor Air Pollution and Asthma,"** ***American Journal of Respiratory and Critical Care Medicine*** **149: 1400-1406, 1994 [Issue 79, Item 31]**

In this study, 164 asthmatics recorded daily exposure to use of gas stoves, woodstoves, fireplaces and ETS and the occurrences of several respiratory symptoms, nocturnal asthma, medication use and restrictions in activity. The authors conclude that exposures to these indoor sources of air pollution are associated with statistically significant increases in the frequency of various asthma symptoms.

EXCERPTS:

"There have been numerous controlled exposure investigations of the pulmonary effects of specific air pollutants on asthmatics. However, relatively few epidemiologic studies have examined relationships between asthmatic status and exposure to both indoor and outdoor sources of air pollution. Although there is abundant clinical evidence of the effects of exposure to indoor aeroallergens, the symptomatic impacts of other common indoor air pollutants from gas stoves, wood stoves, fireplaces, and environmental tobacco smoke have been less well characterized. ... This paper describes an analysis of the associations between indoor and outdoor exposures and several measures of respiratory morbidity in a population of adult asthmatics residing in the Denver, Colorado, metropolitan area during the winter of 1987-1988."

"Exposure to domestic environmental tobacco smoke and to occupational irritants also exhibited statistically significant associations with both moderate cough and shortness of breath."

"Reporting the presence of smokers in the home on the intake questionnaire was associated with an increase in daily moderate or severe shortness of breath (OR, 2.05; 95% CI, 1.78-2.40), as was the reporting of use of a wood stove or fireplace for heating during the year (OR, 1.28; 95% CI, 1.12-1.45)."

"The results of this analysis suggest that both outdoor air pollution and indoor sources of combustion can exacerbate asthma and cause several adverse health outcomes in a population of adult asthmatics. In a previous study, we found that, among the measured outdoor air pollutants, ambient airborne acidity was most consistently related to the occurrence of moderate or severe cough and shortness of breath. This analysis focused on the impact of several indoor sources of pollution: gas stoves, residential environmental tobacco smoke, fireplaces or wood stoves, and occupational exposures."

"Our results showed a strong association between daily use of a gas stove and moderate or severe shortness of breath. . . . For exposure to environmental tobacco smoke, the intake indicator variable of a smoker in the home generated effects of similar magnitude to the reports of daily exposure."

"To our knowledge, our analysis is the first empirical demonstration of the effect of wood smoke on daily symptoms in adult asthmatics. . . . Backdrafting of smoke into the home is common because of inadequate

chimney updrafts, which are due largely to architectural deficiencies. Woodsmoke contains a variety of respiratory irritants, including aldehydes, nitrogen oxides, sulfur oxides, acidic aerosols, and particulates. Several of these compounds have been measured in residences and found to increase with the use of a fireplace or wood stove. Thus, the relationship of wood combustion to asthmatic symptoms reported here is not only intuitive but plausible."

"This investigation documents a strong daily relationship between exposure to cigarette smoke and increased probabilities of clinically significant symptoms in free-living asthmatic adults. As such, it supports previous studies linking exposure to smoke and asthma exacerbations."

[3] **Tashkin, D.P., Detels, R., Simmons, M., Liu, H., Coulson, A.H., Sayre, J., and Rokaw, S., "The UCLA Population Studies of Chronic Obstructive Respiratory Disease: XI. Impact of Air Pollution and Smoking on Annual Change in Forced Expiratory Volume in One Second,"** ***American Journal of Respiratory and Critical Care Medicine*** **149: 1209-1217, 1994 [Issue 77, Item 35]**

Although this study focused in large part on smokers, data presented in the paper suggest that outdoor air pollution may have a detrimental effect on lung function in nonsmokers.

EXCERPTS:

"We assessed the relative impact of residential exposure to community air pollution and habitual cigarette smoking on lung function by comparing the annualized rate of change in forced expiratory volume in 1 s (FEV_1) in current, former, and never-smokers 25 to 59 yr of age residing in three demographically similar areas of the Southern California air basin who had been chronically exposed to (1) moderate levels of photochemical oxidants and very low levels of other pollutants (Lancaster); (2) very high levels of photochemical oxidants, sulfates, and particulate matter (Glendora); and (3) high levels of sulfates, oxides of nitrogen, and probably hydrocarbons (Long Beach), together with moderate levels of sulfur dioxide."

"The University of California at Los Angeles (UCLA) Chronic Obstructive Respiratory Disease (CORD) study has provided the opportunity to compare changes in lung function test parameters over time in several cohorts of smokers and nonsmokers residing in areas of the Southern California air basin chronically exposed to different levels and types of air pollution. In this study we assess the relative impact of residential exposure to community air pollution and habitual cigarette smoking on lung function by comparing the annualized rate of change in FEV_1 in current and never-smokers 25 to 59 yr of age living in three areas of the Southern California air basin, who have been chronically exposed to different mixes of primary and secondary air pollutants."

"In female nonsmokers, residence in either of the two most polluted areas was associated with a significantly greater annual decline in FEV_1, as well as significantly greater percentage of residents with large declines in FEV_1, compared with living in a relatively clean area. . . . The reason for the disparate findings in men and women is unclear, but it may be due to one or more of the following factors: (1) variability in the data; (2) a larger decree of misclassification on smoking status among women because of reluctance of the more health-conscious women to admit to heavy smoking; (3) a difference in the distribution of the intensity or duration of smoking among women in favor of heavier smoking in female residents of the 'clean' area; (4) the exceptional finding of a lower baseline FEV_1 in retested versus nonretested, nonsmoking women residing in one of the polluted areas (Glendora), as discussed below; or (5) different ambient air pollution exposure profiles among women. It is also possible that area of residence had a deleterious effect on the smaller airways of women that would not be detected by changes in FEV_1, is a relatively insensitive indicator of respiratory bronchiolitis."

"The average unadjusted annual decrements in FEV_1 among the never-smoking male and female residents of Lancaster, the least polluted area (37.0 and 32.3 ml/yr, respectively); were higher than the declines that have been reported among nonsmoking adults in some previous population studies. . . . Although we looked intensively for methodologic problems that may have caused the relatively large rates of decline that we observed in nonsmoking adults residing in a relatively 'clean' area, we were unable to identify any consistent factors that would account for the magnitude of decline observed in FEV_1. One possibility is that these relatively large average annual declines in FEV_1 may reflect the accumulated respiratory effects of chronic exposure to ozone and other oxidant pollutants in Lancaster, where the levels of oxidants, although lower than in most other areas of the Southern California air basin, are still higher than in most urban areas in the United States."

"It is interesting that, among never-smoking men and women and current male smokers, annual declines in FEV_1 were significantly greater in those who resided in the community exposed to high levels of sulfates, oxides

of nitrogen, and probably hydrocarbons and moderate levels of sulfur dioxide, but low levels of ozone (Long Beach), than in residents of the community exposed to very high levels of photochemical oxidants, sulfates, and TSP, but low levels of sulfur dioxide (Glendora); at the same time, declines in FEV_1 among residents of both of these communities were significantly greater than in those residing in the area exposed to moderate levels of photochemical oxidants and very low levels of other pollutants (Lancaster). . . . [C]omparison of the results from the three communities suggests that chronic exposure to moderate to high levels of photochemical oxidants in community air may be less damaging than exposure to moderate to high levels of other chemical pollutants, such as TSP, sulfates, NO_2, and SO_2."

"To further assess the relative impact of smoking versus exposure to community air pollution on lung function change, we compared declines in FEV_1 between nonsmokers residing in one or the other or both of the more polluted areas and smokers residing in the least polluted area. Results of this comparison revealed similar declines in FEV_1 between smokers residing in Lancaster and nonsmoking residents of Long Beach and/or Glendora for both mean and women . . . In fact, the mean declines in men and women together were slightly, although not significantly, larger for the nonsmokers residing in the more polluted areas than for the smoking residents of the least polluted area (55.0 versus 53.1 ml/yr, respectively). These findings provide further support for the importance of air pollution exposure to lung function decline relative to the well-recognized effect of smoking."

"In summary, findings from the present study indicate that, in men, the impact of chronic residential exposure to air pollution on decline in lung function appears to be independent of and additive to that of tobacco smoking, suggesting that at least male cigarette smokers residing in areas exposed to high levels of atmospheric pollution may be at particularly high risk of developing functional respiratory impairment. The possibility that long-term residential exposure to heavy air pollution may lead to the development of clinically significant chronic obstructive pulmonary disease in the absence of cigarette smoking, as opposed to simply encroaching on the considerable reserve function of the lung, requires further investigation. Public health professionals in the United States have appropriately given smoking intervention high priority. Our studies suggest that equal priority should probably be given to vigorously intervening in the generation of air pollution as well."

Respiratory Diseases and Conditions -- Children

[1] Bjorksten, B., "Risk Factors in Early Childhood for the Development of Atopic Diseases," *Allergy* 49: 400-407, 1994 [Issue 80, Item 35]

This review focuses on recent reports that allergic diseases are increasing in prevalence in children. The author suggests that the "only definite measure" for reducing the incidence of allergic diseases and asthma is to eliminate exposure to tobacco smoke.

EXCERPTS:

"Several epidemiologic studies in recent years have indicated that the prevalence of allergic diseases is increasing, at least in children and young adults."

"[T]he indoor environment probably plays as large, if not a larger, role [than outdoor pollution] in the development of allergic sensitization and the appearance of allergic disease in the sensitized person."

"This review discusses various risk factors encountered in early childhood that may influence the development of allergic disease."

"Passive smoking is by far the most documented risk factor for the development of allergic disease. This is particularly true in early childhood, independently of how 'allergy' is defined. Numerous epidemiologic studies have found an association between exposure to tobacco smoke and recurrent wheezing, bronchial hyperreactivity, and the diagnosis of asthma. An association between passive smoking and an increased risk of sensitization to environmental allergens has also been shown, in both clinical studies and animal experiments. There is little doubt that exposure to tobacco smoke is the most important environmental risk factor for childhood allergy and respiratory disease identified so far. The long-term effects of childhood exposure to tobacco smoke are unknown."

"While there is convincing evidence of an association between exposure to tobacco smoke and childhood allergy, the role of smoking during pregnancy is less clear. Although there are reports of an association between maternal smoking and childhood allergy, the studies are inconclusive because of their design. Infants of smoking mothers are, however, exposed to significant amounts of nicotine in breast milk."

"Whether the Western lifestyle is associated with an introduction of new, unknown adjuvants enhancing sensitization, or whether factors that are necessary for the induction of tolerance are absent is not known. Efforts

during infancy to effect primary long-term prevention of allergic disease have largely failed and are probably based on an incorrect hypothesis. Thus, it seems likely that avoidance of exposure to allergens is antigen specific, and avoidance of, say, allergenic foods in infancy would result only in less allergy to that particular food, and not in any reduction of, say, allergy to inhaled allergens."

"The only definite measure to reduce the general risk of allergy and asthma is carefully to avoid all exposure of infants and young children to tobacco smoke. In addition, avoidance of certain allergens for the first years of life may reduce the incidence of sensitization to that particular antigen."

[2] Brugman, S.M., and Larsen, G.L., "Childhood Asthma: Wheezing in Infants and Small Children," *Seminars in Respiratory and Critical Care Medicine* 15(2): 147-160, 1994 [Issue 80, Item 34]

In this review paper, the authors discuss diagnosis, drug treatment, and environmental controls for the management of asthma in very young children. They call elimination of ETS exposure "the single most important and achievable goal" in terms of environmental modifications for asthmatics.

EXCERPTS:

"This review will focus . . . on asthma in the infant and very young child."

"The impact of environmental control measures in asthma management should not be underestimated. Of all the factors that impact on asthma, some are genetically determined and are therefore difficult to alter. Of those factors that can be manipulated, environmental elements predominate. Any intervention that could weight the scales in favor of the 'no wheeze' side has potential for attenuating, and perhaps preventing, the expression of asthma."

"Eliminating cigarette smoke exposure is the single most important and achievable goal in this regard. As early as the prenatal period, passive smoke exposure has been shown to have multiple deleterious effects, including increasing IgE levels, increasing the prevalence of eczema, retarding intrauterine growth, and altering the developing lung so that baseline lung function is reduced at birth. Postnatal smoke exposure is associated with lower respiratory tract illness, wheezing, more frequent hospitalization, and a fourfold increase in BHR [bronchial hyperresponsiveness]. This association is much more compelling when it is the mother who smokes rather than the father. In addition, smoking-induced wheezing appears to be dose related so that both the incidence of wheezing in children and its severity are related to the number of cigarettes smoked. Eliminating this potent irritant in all phases of life might go a long way to prevent asthma."

"Other irritants in the environment include smoke from wood-burning stoves and fireplaces, gaseous emissions from gas (carbon monoxide [CO] and nitrogen dioxide [NO_2] and kerosene stoves (CO, NO_2, and sulfur dioxide) as well as automobiles (CO, NO_2, ozone, and volatile organic compounds), households products such as cleaning agents, bleaches, perfumes and glues, and odors from solvents, paints, and other agents in home. . . . [T]he accumulation of indoor air pollutants is intensified, presenting a modern hazard to the child with reactive airway disease."

[3] Charlton, A., "Children and Passive Smoking: A Review," *The Journal of Family Practice* 38(3): 267-277, 1994 [Issue 76, Item 36]

This review article, which cites 199 references, claims that ETS exposure is associated with a number of health endpoints in children, including respiratory conditions and otitis media.

EXCERPTS:

"Effects of maternal smoking on the fetus include low birthweight, increased risk of spontaneous abortion, and perinatal death. The effect of maternal smoking on breast feeding is still enigmatic. Breast-fed infants of mothers who smoke appear to be protected against respiratory diseases but are subjected to chemicals from the smoke transferred in the milk. It is difficult to separate prenatal and postnatal effects with regard to growth, development, and lung function retardation. There is, however, a definite increase in respiratory diseases, otitis media, and minor ailments, which are unequivocally related to parental, especially maternal, smoking."

"The purpose of this paper is to examine the evidence and to present a review of current knowledge with regard to children and passive smoking."

"There is now evidence that passive smoking by the mother during her pregnancy as a result of her partner's smoking is also related to the baby being small for gestational age. There has also been at least one report of sperm damage caused by the father's smoking."

"It is often impossible to separate the effects of exposure of the fetus to smoke from those of passive smoking after birth because problems of early childhood can be both developmental and environmentally induced."

"It is in the area of respiratory disorders and symptoms that the case against passive smoking is probably most conclusive."

"Although early studies associated passive smoking with respiratory illness only in infants, research is now showing a continued effect through primary school to adolescence."

"When assessing the effect of passive smoking, it is important to take into account factors such as type and size of house, urban or rural location, type of cooking fuel used, and health history of the family. Even when all these confounding elements are accounted for, most research has shown that passive smoking is still associated with a higher risk of respiratory problems."

"There is little evidence that passive smoking causes asthma in children, but considerable evidence that it exacerbates a preexisting asthmatic condition."

"There have been more than a dozen studies on lung function in children in relation to exposure to parental smoking, which have revealed an overall reduction of 1% to 5% lung volume."

"The changes in lung function observed so far are not large enough to be considered illnesses, but definitely are associated with passive smoking."

"The effect of ETS on a child's long-term growth and development is still relatively unclear. There are a number of reasons for this uncertainty, including the initial effect of low birthweight and the genetic, social, and cultural factors that interact in the developmental processes."

"Very few of the numerous studies carried out in the last 10 years on the risk of middle ear effusion related to passive smoking have not found a significant association, and it can now be stated conclusively that exposure to environmental tobacco smoke in the home and in daycare increases the risk of middle ear effusion in children. Overall, one third of the gases of 'glue ear' can be attributed to parental smoking."

"There is preliminary evidence of changes in the cardiovascular system of children exposed to passive smoke."

"When as many factors as possible were accounted for, at least three studies have shown positive links between passive smoking in childhood and lung cancer in later life."

"Based on the numerous excellent and detailed reviews of passive smoking effects in general and on the fetus, infants and children in particular that have been published over the past 10 years, the fact that children's health is at risk because of passive smoking is unquestionable."

[4] Cunningham, J., Dockery, D.W., and Speizer, F.E., "Maternal Smoking During Pregnancy as a Predictor of Lung Function in Children," *American Journal of Epidemiology* 139(12): 1139-1152, 1994 [Issue 76, Item 37]

In this paper, the authors claim that maternal smoking during pregnancy or early in a child's life may be associated with long-term decrements in pulmonary function.

EXCERPTS:

"This study examined the relative magnitude of the effects of maternal smoking during pregnancy and later childhood environmental tobacco smoke exposure on the lung function of 8- to 12-year-old children."

"The current analysis focuses on FEV_1, FVC, the ratio of FEV_1 to FVC (FEV_1/FVC), forced expiratory volume at 3/4 of a second ($FEV_{0.75}$), peak expiratory flow rate (PEFR), $FEF_{25-75\%}$, and the average forced expiratory flow rate between 65 and 75 percent of FVC ($FEF_{65-75\%}$)."

"Children exposed to passive smoke in utero were significantly shorter,heavier, and older than were children who were not exposed. Similar differences were observed for maternal smoking in the year prior to the examinations. Smoking in the home by the child's father or another primary adult was significantly more common for children whose mothers smoked during pregnancy or in the year before the study, as was smoking in the home by others (including regular visitors)."

"After adjusting for several potential confounders, we found that the child's exposure to maternal smoking during pregnancy was associated with deficits of 1.8 percent in $FEV_{0.75}$, 1.4 percent in FEV_1, 1.3 percent in FEV_1/FVC, 2.1 percent in PEFR, 5.2 percent in $FEF_{25-75\%}$, and 6.8 percent in $FEF_{65-75\%}$. There was no significant difference in FVC. Recent maternal smoking was associated with smaller deficits in $FEV_{0.75}$, FEV_1, FEV_1/FVC, PEFR, $FEF_{25-75\%}$, and $FEF_{65-75\%}$. No difference was observed for FVC."

"The estimates for the effect of current environmental tobacco smoke exposure from maternal smoking were greatly reduced after controlling for prenatal exposure . . . and were no longer statistically significant."

"Controlling for current smoking in the home by the father (or other primary adult) and others did not substantially change the size of any estimate. In addition, there was no consistent evidence of an association between current paternal smoking or current smoking by others in the home and the lung function of children, even for children of never-smoking mothers."

"A persistent deficit in lung function that was associated with maternal smoking during pregnancy and that was not explained by current maternal smoking alone was observed in the children. The effects were observed primarily in measures of flow rather than volume, suggesting that changes involve the obstruction of airways. Exposure to maternal smoking in utero is qualitatively different from postnatal environmental tobacco smoke exposure. Prenatal exposure to maternal smoking is restricted to those components of mainstream smoke inhaled by the mother that eventually cross the placenta. Environmental tobacco smoke exposure during childhood, on the other hand, results from the combination of sidestream smoke and smoker-exhaled mainstream smoke, which may act directly on the respiratory system. Thus, the health effects associated with in utero environmental tobacco smoke exposure may be attributable to a different component of tobacco smoke than those associated with later, postnatal environmental tobacco smoke exposures. . . . Although the evidence is weak, these data suggest that flow measurements may be affected by environmental tobacco smoke within the first trimester of pregnancy, a period during which much of the development of the bronchial tree takes place. Thus, the evidence for long-term deficits in flow associated with maternal smoking during pregnancy, even among children whose mothers are no longer smoking, is consistent with what is known about lung development."

"One limitation of the current study, however, is that it does not allow for a satisfactory distinction between passive smoke exposure in utero and environmental tobacco smoke exposure in the early postnatal period. It is rare that a mother who smoked during pregnancy would quit on the birth of her child. Even so, these results suggest a residual effect of prenatal and perhaps early postnatal environmental tobacco smoke exposure."

"The hazards of personal smoking have been well documented, and the risks of environmental exposures to others' smoking are being recognized. The evidence presented here suggest that exposure to maternal smoking during pregnancy (and/or very early in life) may produce long-term, potentially irreversible decrements in lung function. Such delayed effects of prenatal exposure reaffirm the importance of educational intervention aimed at prevention or cessation of smoking, particularly among women contemplating pregnancy."

[5] Gross, A.J., "Respiratory Disease and ETS." In: *Environmental Tobacco Smoke.* H. Kasuga (ed.). Springer-Verlag, 85-107, 1993 [Issue 81, Item 19]

The author of this review concludes that risk estimates for respiratory illness in children exposed to ETS should not be made. He cites inconsistencies in the studies in this area, inadequacy of treatment of confounders, and lack of data on a possible mechanism as particular difficulties.

EXCERPTS:

"The essential question, and the basis of this presentation, is whether the EPA's conclusion regarding ETS and the respiratory health of children, as well as the corresponding risk estimates, have a firm scientific grounding. In my opinion, the scientific data do not support the conclusions of the EPA. I base this conclusion on the objective analyses of the relevant pediatric respiratory literature performed by Witorsch, Hood, and coworkers as well as an independent survey of key papers in this field that I have conducted."

"While the association between parental smoking and respiratory illness in young children appears consistent, no such consistency exists for respiratory illness, pulmonary function in school age or older children, or middle ear disease at all ages. Systematic analyses of the relevant literature reveals [sic] some common characteristics in the way in which potential confounding variables and other aspects of study design have been treated in epidemiologic studies of parental/household smoking and the respiratory health of preschool and school-age children. With regard to particular confounding variables considered, SES, gender, and age were represented in three-fourths or more of both groups of studies. Similarly, the set of confounding variables that have been neglected (i.e., represented in one-quarter or less, or not at all) is the same in both age groups, namely indoor pollution, day care attendance, animal exposures, stress, dampness/cold, occupational exposures, and nutritional status. It is noteworthy that maternal smoking during pregnancy, which was addressed only in the group of studies in preschool children, was represented in only four such studies."

"The epidemiologic studies of both age groups reveal a wide variation from study to study in the array of confounders considered, and most individual studies consider too few confounders. For example, only three of 41 studies in preschool children considered 50% or more of available potential confounders. It should also be a matter of concern that such a large proportion (50-75%) of the clinical endpoint studies in both age groups of children lack verification of such endpoints."

"Analysis of individual confounding variables also revealed in both sets of studies that there was considerable variation in the criteria used to characterize these confounding variables (such as SES, family health history, personal health history and age). Furthermore, the way in which these confounders were controlled, if at all, varied from study to study."

"The fact that several confounding variables were found to be consistently *not* associated with an endpoint or to provide equivocal results in both age groups deserves comment. In some of these cases (such as SES, gas stove usage, and type of infant feeding) this lack of association is inconsistent with the results of other studies and/or appears to be counterintuitive. While this may reflect a lack of effect of such variables on the respiratory system, it is possible that this could also reflect the lack of standardization in the criteria used for each confounder, the specific clinical endpoints considered and their validation, not to mention the variability of statistical methodologies used in these studies."

"The fact that six confounders to date have been identified in preschool children that are consistently associated with increased risk of respiratory illness is important since they may have an impact on the putative association between ETS exposure and prevalence of disease in this age group. Butler also suggests that variables that are not significantly and independently associated with outcome could still have a confounding effect on the result."

"While several reports, including that recently published by the U.S. EPA, attempt to convey the impression that the issue of confounding variables in this literature has been resolved, a thorough analysis of the literature reveals that attention to confounding variables is inadequate and lacks rigor in the following ways: 1) the consistency with which they have been considered from study to study; 2) the criteria that have been used to characterize such variables; 3) omissions of some potentially important variables; 4) lack of standardization with regard to the array of confounders considered; and 5) lack of standardization of the methodology used to adjust for confounders."

"The foregoing design flaws raise a compelling question as to whether the association between parental/household smoking and respiratory illness in young children can legitimately be attributed to ETS as opposed to a confounding factor or a combination of several confounders. One such factor that deserves future consideration is the possibility of *in utero* effects of maternal active smoking during pregnancy, an issue addressed in only four of the 41 relevant studies. In fact, the EPA report itself presents evidence that supports a possible *in utero* mechanism for presumed ETS effects."

"In view of the inconsistencies in the database pertaining to older children, the inadequate attention that has been paid in all studies to potentially important confounding variables, and the lack of compelling scientific evidence establishing an ETS-mediated mechanism for the association between ETS and respiratory illness in young children, risk estimates are both premature and inappropriate."

[6] Horstman, D., and Vitnerova, N., "Respiratory Tract Status of School Children Living in High Polluted [sic] and Control Areas in Czech Republic," *Zentralblatt Hyg Umweltmed* 195: 203, 1994 [Issue 77, Item 36]

Data from children in two areas of the Czech Republic are reported in this meeting abstract. The authors claim that asthma, chronic bronchitis, and allergic diseases are more common in the children living in a polluted area. They also claim that respiratory tract symptoms, such as cough, occur more frequently in families with smokers.

EXCERPTS:

"The authors evaluated 3000 Teplice and 1500 Prachatice (control area) questionnaires about respiratory status of 2, 5, and 8th grade elementary school children. Teplice district is one of the most polluted areas in Europe and Prachatice district serves as a control. A randomly selected group of 1000 children from both districts was spirometrically examined during autumn and spring season. The data analysis shows that children from the polluted area have a significantly higher prevalence of asthma, chronic bronchitis and allergic diseases. There are significantly higher numbers of respiratory tract symptoms, especially morning cough and wheezing. These symptoms occur more often in smoking families."

"The respiratory function values show seasonal variability. Children from the polluted area have expiratory parameters both flow and volume lower and the values measured are more spread. The distribution curve of volume and flow expiratory parameters by children from smoking families show a shift to lower values in both districts."

[7] Kahn, A., Groswasser, J., Sottiaux, M., Kelmanson, I., Rebuffat, E., Franco, P., Dramaix, M., and Wayenberg, J.L., "Prenatal Exposure to Cigarettes in Infants with Obstructive Sleep Apneas," *Pediatrics* 93(5): 778-783, 1994 [Issue 76, Item 38]

Although the authors of this paper claim that maternal smoking during pregnancy was associated with an increase in the frequency and duration of infants' sleep apneas, they report no association for paternal smoking alone. They do claim an increased risk for both maternal and paternal smoking during pregnancy.

EXCERPTS:

"To evaluate the influence of prenatal parental smoking on infant cardiorespiratory behavior during sleep, 550 apparently healthy infants were studied in pediatric sleep laboratories."

"Comparing the infants of nonsmokers, light smokers, and smokers, the proportion of infants with obstructive sleep apneas increased from 40.5% to 48.6%, and to 65.3%, respectively. The duration of the obstructive apneas was significantly related to the number of cigarettes smoked daily during pregnancy."

"For the 394 infants studied in the postnatal age, the number of cigarettes smoked by the mothers after their child's birth was not associated with an increased frequency in obstructive sleep apneas. Likewise, no increase in obstructive apnea frequency was found in the infants exposed longer to environmental cigarette smoke (the 152 infants aged between 12 and 39 weeks)."

"The frequency of obstructive sleep apneas was not related to the number of cigarettes smoked by the fathers alone, either before or after pregnancy. However, the cumulative effect of smoking by both smoking fathers and mothers during pregnancy lead to an increase in the number of infants with obstructive apneas from 19.5% to 36%."

"The association found between smoking during pregnancy and increased frequency of and duration of obstructive sleep apneas in newborns and infants has not been shown previously. This correlation has a dose-response pattern and seems to occur prenatally, as can be suspected from the following observations. The neonates of smokers had not yet been exposed to environmental cigarette smoke because smoking was strictly prohibited in the hospital and nursery. . . . Smoking by the mothers after their child's birth was not associated with an additional risk for obstructive apneas. Additionally, in the postneonatal group, infants showed no increase in apnea frequency with duration of exposure to ambient smoking."

"Paternal smoking during pregnancy added to the risk of obstructive apneas in the infants of smoking mothers, but smoking in the postnatal period did not seem to have such an effect."

"The clinical significance of the observed sleep apneas is unknown. . . . It can only be speculated whether our findings concur with the present understanding of the mechanisms contributing to some sudden infant death syndromes (SIDS)."

[8] Meinert, R., Frischer, T., and Kuehr, J., "The 'Healthy Passive Smoker': Relationship Between Bronchial Hyper-Reactivity in School Children and Maternal Smoking," *Journal of Epidemiology and Community Health* 48: 325-326, 1994 [Issue 81, Item 20]

Based on results of a cross-sectional study, the authors of this brief paper suggest that effects may be underestimated in such a study if changes in exposure status are not considered. For instance, their data suggested a decreased risk of bronchial hyper-responsiveness in children whose mothers smoked, compared to asthmatic children of nonsmokers, which they suggest is related to failure to document changes in smoking status.

EXCERPTS:

"We present data from a cross sectional study on the association between maternal smoking and bronchial hyper-reactivity (BHR) in 1401 8 year old school children, in whom the phenomenon of 'healthy passive smokers' was observed."

"Ninety two children (6.6%) had BHR. Of 162 asthmatics, 25 (15.4%) had BHR. There was a positive association between BHR and maternal smoking before pregnancy, during pregnancy, and in the children's 1st year of life, but not for the children's 8th year of life."

"Between the child's 1st and 8th year, 7.6% (asthmatics: 0%) of mothers of children with BHR compared with 11.3% (asthmatics: 11.7%) of mothers of children without BHR began smoking, while 7.6% (asthmatics: 16.0%) of mothers of responsive children stopped smoking compared with 3.4% (asthmatics: 2.9%) of those with unaffected children. This association between BHR and changes in maternal smoking habits was significant."

"Our data suggest that mothers of children with BHR, especially mothers of asthmatic children, seemed less likely to take up smoking. Furthermore, the occurrence of BHR obviously stimulated mothers to quit smoking. Hence, the use of the term 'healthy passive smoker' seems to be justified, although possible biases exist. We can only speculate about the true inter-relation between exposure and disease, since we do not know when a child developed BHR for the first time."

"If there is a mutual inter-relation between exposure and disease, the analysis of the relationship between current exposure and disease can easily give misleading results. For example, not taking information on prior passive smoke exposure into account, our data would suggest that

eight year old asthmatic children of currently smoking mothers have only half the risk of developing BHR, as have asthmatic children of non-smoking mothers. We conclude that in cross sectional studies investigating long term exposure there is a high risk of underestimating effects if only information on current exposure status is available. In order to assess the true exposure-disease relationship it seems important to acquire information on status of exposure at different prior points in time as well, and, if possible, on disease status at prior points in time."

[9] **Neuberger, M., Kundi, M., and Wiesenberger, W., "Lung Function and Chronic Exposure to Air Pollution at School Age," *Zentralblatt Hyg Umweltmed* 195: 202, 1994 [Issue 77, Item 37]**

In this meeting abstract, the authors claim that, in their sample of more than 15,000 children, exposure to "passive smoking" was associated with lung function decrements that remained over the five years of the study.

EXCERPTS:

"Most studies on air pollution and lung function have been restricted to highly selected groups or limited to short term effects. We tested the hypothesis whether indicators of long term outdoor and indoor air quality are associated with lung function by examining all elementary and high school children of a town by standardized methods (questionnaire, medical checkup and flow-volume measurements) and relating data of 15,045 non-smoking participants 6-16 years of age cross-sectionally to outdoor air pollution measurements from the nearest of 9 monitoring stations in the year preceding the spirogram and to domestic exposure to tobacco smoke, gas-cooking and heating reported. Partial correlation coefficients were significant for different lung function parameters and SO_2, total suspended particulates (TSP), NO_2, passive smoking and cooking with gas. Indications for long-lasting effects of outdoor NO_2 (motor traffic, chemical industry, etc.) and TSP combined with SO_2 (steel industry, heating, etc.) on small airway function were found. Canonical correlation analysis put more weight to TSP as indicator of outdoor pollution and to passive smoking as indicator of indoor pollution. In all multivariate analyses considering confounders only the higher outdoor pollution during winter months showed negative effects on lung function while long lasting effects of summer pollution (ozone) could not be proven. The only negative influence which showed no improvement during the 5 years of observation was passive smoking which is all the more worrying because its main target seem[s] to be peripheral airways as indicated by small but significant impairments of end expiratory flow rates."

[10] **Spengler, J., Neas, L., Nakai, S., Dockery, D., Speizer, F., Ware, J., and Raizenne, M., "Respiratory Symptoms and Housing Characteristics," *Indoor Air* 4: 72-82, 1994 [Issue 81, Item 21]**

As part of a survey of more than 15,000 children in 24 American cities, questions were asked concerning a number of exposures and lower respiratory symptoms. The authors report statistically significantly elevated risk estimates for living in an older home, living with smokers, having an air conditioner, having an air cleaner, having a humidifier, home dampness, and the presence of mold and water.

EXCERPTS:

"A comprehensive questionnaire was completed by 15,523 children living in 24 North American communities. . . . The survey was designed to examine prevalence of respiratory symptoms and pulmonary performance among school-age children, 9-11 years old, and community exposures to ozone, particles (PM_{10}), and acidic and gaseous air pollution. An inventory of home appliances, fuel types, air conditioning (cooling, humidifying), pets and building descriptors provides an opportunity to explore the relationships to health variables and intrinsic conditions (e.g. atopy)."

"[V]ariables were derived from combinations of several symptoms. The composite variable of asthmatic symptoms . . . bronchitic symptoms . . . and lower respiratory response . . . are featured in this analysis."

"More symptoms are reported for boys, by better-educated parents, and for children living in older homes. Parental respiratory health status is an important predictor of childhood health. Atopic children and children who experienced a serious respiratory illness before age two report substantially more symptoms."

"The presence of air conditioners, air cleaners, and humidifiers has a positive and statistically significant association with all three composite health indicators. Examining the housing factors in more detail reveals a tendency for these appliances to be present together in a home."

"Among the combustion sources, which were gas cooking, wood burning, unvented heaters and current smoking in the home, only current smoking in the home was associated with increased symptoms, odds ratios changing between 1.20 and 1.24 for the three composite symptom variables. Comparing gas stoves with pilot lights to electric range homes or homes that used the gas range to heat did not reveal significant associations."

"Home dampness had a strong association with bronchitic symptoms (1.63) and less so for asthmatic symptoms (1.22)."

"Dampness was negatively associated with mobile homes, use of kitchen fans, and air conditioners. It was positively associated with older homes, use of oven to heat, unvented heaters, humidifiers, and pets."

"The current 24 Cities Study doubles the North American population indicating that the prevalence of dampness conditions is widespread, in the range of 40% to 60%. Further, the association of these conditions with respiratory symptoms is substantial, with odds ratios varying between 1.3 and 2.2. If these associations are real, then moisture and mold conditions within our current housing stock are a substantial contributor to morbidity."

"It is, then, highly probable that the presence of mold, dampness and related conditions in homes are contributing to morbidity. However, we do not have substantial documentation of the extent of these problems within U.S. housing stock. Examining the associations between dampness, mold growth and specific health outcomes will be difficult to study in the field."

[11] **Wang, X., Wypij, D., Gold, D.R., Speizer, F.E., Ware, J.H., Ferris, B.G., and Dockery, D.W., "A Longitudinal Study of the Effects of Parental Smoking on Pulmonary Function in Children 6-18 Years,"** ***American Journal of Respiratory and Critical Care Medicine*** **149: 1420-1425, 1994 [Issue 78, Item 30]**

The authors of this paper, reporting on data from the Harvard Six Cities Study, claim that decrements in pulmonary function in children were associated both with maternal smoking during pregnancy and with current maternal smoking. They claim that such decrements may persist into adulthood and may be associated with risk of COPD.

EXCERPTS:

"What is not known is whether the *in utero* effects of exposure persist beyond infancy, and whether subsequent postnatal exposure in the preschool or school years confer additional risk for decreased level or growth of pulmonary function."

"The Harvard Six Cities Study provides an opportunity to address these issues in a large cohort of children. Utilizing longitudinal follow-up data available on children 6 to 18 yr, this analysis examines the timing and intensity of exposure to ETS and its association with pulmonary function level and growth from childhood through adolescence."

"The growth stage at which a child is exposed to ETS may influence the degree and the manner in which pulmonary function is affected. . . . Studies so far provide little information on the long-term significant of *in utero* and early childhood exposure to ETS on lung growth and development."

"The findings of this study suggest that among school-aged children, the decrement in pulmonary function level associated with maternal smoking appeared to be a combination of a persistent deficit related to earlier (including *in utero*) exposure and an additional deficit related to current exposure. The high degree of tracking shown by the spirometric parameters implies that the decrements in lung function related to early childhood exposure to ETS may persist into at least early adulthood."

"The capacity of the analysis to estimate exposure to ETS prior to the initiation of the study is limited by the retrospective nature of the data and the lack of quantification or knowledge of timing of exposure. . . . [P]recise data regarding the *in utero* ETS exposure is missing from this data set."

"Between ages 6 to 10 yr our ability to separate current from past smoking experience is limited by the close correlation between past and present smoking habits, as only a small proportion of mothers stopped smoking. Between ages 11 and 18 yr, past and current smoking experiences diverged more; the data strongly support separate, additive effects of ETS exposure in early childhood and current ETS exposure."

"In the present analysis of Six Cities children, only current maternal smoking predicted significantly slower annual growth rates of pulmonary function. In children 6 to 10 yr of age, current maternal smoking was associated with slower growth rates of FVC (-2.8 ml/yr), FEV_1 (-3.8 ml/yr), and $FEF_{25-75\%}$ (-14.3 ml/s/yr) for each pack/d smoked. In children 11 to 18 yr of age, current maternal smoking was associated with slower growth rates of $FEF_{25-75\%}$ (-7.9 ml/s/yr)."

"Consistent with previous studies, the effects of maternal smoking on children's pulmonary function were significant but were small in magnitude. This may be partially attributed to misclassification of exposure. The validity of questionnaire data depends on the subject's ability to accurately recall and report smoking information."

"As observed in previous studies and this present study, maternal smoking had a stronger association with children's pulmonary function than paternal smoking. A plausible explanation is that children are more likely to be with their mothers than with their fathers at the times smoking occurs, especially during early childhood. . . . Alternatively, *in utero* exposure to cigarette components and their metabolites may lead to permanent changes in lung function."

"Our study findings may be important in two respects. First, they suggest the presence of pathophysiologic effects of exposure to maternal smoking on the lungs of the growing child. Second, to the degree that the effects of early ETS exposure persist or accumulate throughout childhood, they may represent important predictors of development of COPD in adult life, particularly among those who take up cigarette smoking themselves."

OTHER CANCER

[1] **Bunin, G.R., Buckley, J.D., Boesel, C.P., Rorke, L.B., and Meadows, A.T., "Risk Factors for Astrocytic Glioma and Primitive Neuroectodermal Tumor of the Brain in Young Children: A Report from the Children's Cancer Group,"** ***Cancer Epidemiology, Biomarkers & Prevention*** **3: 197-204, 1994 [Issue 77, Item 38]**

Two forms of childhood brain tumor were investigated in this case-control study. Although some 200 potential associations were investigated, few statistically significant risk estimates are reported. The authors report that frequencies of maternal and paternal smoking, and of maternal ETS exposure did not differ between cases and controls.

EXCERPTS:

"We conducted a matched case-control study to investigate risk factors for the two most common types of brain tumors in children, astrocytic glioma and primitive neuroectodermal tumor (PNET). Since the study focused on gestational exposures, we restricted it to young children because these exposures would be expected to act early in life. Parents of 155 astrocytic glioma cases, 166 PNET cases, and controls identified by random digit dialing completed telephone interviews. Few associations occurred with the hypothesized risk factors, which were gestational exposure to alcohol, hair coloring products, farms, and substances containing N-nitroso compounds (passive smoking, makeup, incense, new cars, pacifiers, baby bottles, beer)."

"No ORs that were statistically significant or greater than 1.5 were observed for pregnancy exposure to beer, make-up, incense, or new cars, products that contain N-nitroso compounds. Cases and controls did not differ significantly in maternal or paternal cigarette smoking (a major source of preformed N-nitroso compounds) before or during the pregnancy, maternal passive smoking, or daily duration of maternal passive smoking. Rubber baby bottle nipples and pacifiers contain N-nitroso compounds; no substantially elevated Ors were observed for baby bottle or pacifier use or duration of use, although type of nipple was not studied."

"We observed few associations between hypothesized risk factors and the two most common childhood brain tumors, astrocytoma and PNET. The number of significant associations is no more than that expected by chance, given the approximately 200 comparisons made for each tumor type. Nonetheless, several of the findings are consistent with previous observations. In addition, some of the negative findings conflict with those of earlier studies."

"Preston Martin et al. observed increased risk associated with maternal exposure to burning incense, sidestream cigarette smoke, face make-up, diuretics, and antihistamines, which all contain N-nitroso compounds. We did not observe ORs that were statistically significant or greater than 1.4 for any of these exposures. Other studies have reported negative findings for sidestream or paternal smoking, diuretics, antihistamines, face make-up, and incense. The mother's exposure to a new car and the child's use of baby bottles and pacifiers also were hypothesized as risk factors because rubber contains N-nitroso compounds. No effect of these products was observed. Of the products suggested to be risk factors based on their content of N-nitroso compounds, only beer was associated with a significantly increased risk. The association with beer was for PNET only."

"This study had adequate power to detect relative risks of 3.5 for buying a new car and incense burning and of 2.0-2.5 for make-up, passive smoking, and pacifier use. The detectable ORs are slightly lower than those in the study that observed positive associations with these exposures."

"The associations of PNET with farm residence of the mother and child, although only one of the two was statistically significant, are consistent with some previous findings."

"We observed a significant protective effect of maternal history of miscarriage for PNET but not for astrocytoma. . . . These conflicting results are perplexing and perhaps chance explains the protective effects observed."

"We observed a modestly increased risk of astrocytoma associated with a head injury that required medical attention. The OR adjusted for income level was about 2 and approached statistical significance."

"Other factors associated with increased risk for astrocytoma were use of kerosene and birth by Caesarean section. . . . These findings should be investigated again, although given the large number of comparisons made, they may have occurred by chance."

"In summary, few exposures of the mother, father, or child were associated with increased risk of astrocytoma or PENT. Despite case groups that were more homogenous than those of previous studies, we were generally unable to replicate findings related to the N-nitroso hypothesis. Findings deserving of future attention include the association of PNET with farm residence and beer consumption and the association of astrocytoma with head injury, Caesarean section, and kerosene."

[2] **Smith, S.J., Deacon, J.M., Chilvers, C.E.D., and members of the U.K. National Case-Control Study Group, "Alcohol, Smoking, Passive Smoking and Caffeine in Relation to Breast Cancer Risk in Young Women," *British Journal of Cancer* 70: 112-119, 1994 [Issue 78, Item 31]**

Based on a subset of data collected on young breast cancer cases and their controls in the United Kingdom, the authors report no consistent elevation or dose-response trend for breast cancer risk associated with ETS exposure. They conclude that, based on these data and on their data suggesting no increased risk among *active* smokers, that an effect of ETS exposure on breast cancer is "implausible."

EXCERPTS:

"The UK National Case-Control Study Group (UKNCCSG) was set up primarily to investigate the relationship between oral contraceptive use and breast cancer risk in young women. Data were also collected on lifestyle factors such as smoking, alcohol consumption and caffeine consumption. We also investigated the relationship between breast cancer risk and passive smoking in response to findings reported by Sandler et al. who found passive smoking to be a significant risk factor for breast cancer. For this part of the study an additional questionnaire on lifetime passive smoking exposure was sent to a subset of women in the main study."

"In the passive smoking study, significant differences between cases and controls were found in the crude relative risks for family history of breast cancer, parity and history of breastfeeding. Relative risks associated with oral contraceptive use were also very similar to the results of the main study, but did not reach conventional levels of significance because of the smaller numbers. All these factors, and the established parity-related risk factors for breast cancer, have been adjusted for in our analysis. Because of the possibly complex effects of confounding and interaction between active and passive smoking, the risks associated with passive smoking were also examined in an unmatched analysis of non-smokers alone."

"Most relative risks for passive exposure to cigarette smoke were slightly in excess of unity. For total lifetime exposure, risks were statistically significantly raised, but there was no evidence of a trend with increasing exposure. The increased relative risks were due to a deficit of cases who had never been exposed (16 cases and 28 controls never exposed in childhood or from a partner) rather than an increasing risk with increasing exposures. There was no evidence of a significant trend for any of the individual exposure variables examined. The trend test for period of exposure (classified as never, childhood, adult or both childhood and adult exposure) was significant, again because of a deficit of cases never exposed (six cases and 14 controls never exposed at any time). The relative risk from exposure to maternal smoking was close to unity (RRs = 0.98 and 0.99 for 1-200 and more than 200 cigarette years of exposure respectively)."

"The matched analysis of 170 case-control pairs gave slightly lower RRs generally but marginally significant trends with increasing exposure in childhood and over the total lifetime were found. RRs for more than 400 cigarette-years of exposure in childhood and over the whole lifetime were 1.90 (95% CI 0.73-4.92) and 2.54 (95% CI 0.88-7.36) respectively."

"Interactions between total childhood exposure and own smoking history and between total lifetime exposure and own smoking history were also investigated. There was no statistical evidence for heterogeneity between smokers and nonsmokers for either of these two exposures (data not shown)."

"The results from the unmatched analysis in non-smokers, in which there were 94 cases and 99 controls, were very similar to those for the whole dataset. Relative risks were consistently slightly elevated, but confidence intervals were wide and included unity. There was no evidence of a significant dose response for any of the exposure variables."

2046343780

"In this study we have failed to demonstrate an association between own smoking and breast cancer in young women. Risk estimates were close to unity, and there was no evidence of any dose-response relationships."

"We failed to demonstrate a significant trend in breast cancer risk with passive smoking exposure. Estimates of relative risks for many of the measures of exposure were, however, consistently raised, some point estimates approaching conventional levels of significance, and there was a significant trend with period of exposure and a relative risk of 3.13 for exposure during both childhood and adulthood. Tests for trend in the matched analysis were also of borderline statistical significance. The numbers of women never exposed were, however, very small. There are, however, explanations for the findings other than a causal association, such as information or recall bias; this may particularly affect the validity of questionnaires applied for self-completion after participation of the subjects in a major structured interview concerning the same disease."

"Sandler et al. reported a consistent association between adult and total lifetime passive smoking exposure and breast cancer risk but included fewer than 60 women with breast cancer among a total of approximately 500 male and female cases with cancer at any site. These women were compared with an unstated number of female controls, 60% of whom were friends of study cases, the remainder being selected from the community using the technique of random digit dialling. The analysis was controlled for age and level of education only. The cases included were aged up to 59 years rather than up to 35 as in the current report."

"The odds ratios reported for breast cancer by Sander et al. were of a similar magnitude to those found in the current study, being 1.8 for women ever married to a regular smoker (95% CI 1.0-3.7), and rising to 3.3 for women with three or more household exposures during their lifetime, the trend being significant. The validity of [the] Sandler et al. studies is difficult to assess because the reports were brief. The finding of such highly significant results is surprising in view of the fact that only very small numbers of cases were included. The prevalence of passive smoking exposure in the control group was not given but must have been rather low, suggesting that controls may not have been representative of the general population, in which prevalence of household exposure has been found to be of the order of 70% in this age group. The study methods used, therefore, may have been subject to bias; the use of friend controls may have introduced serious information bias, and while the non-repose rate in cases was quoted at only 16%, that in controls was not documented, raising the possibility of selection basis. The effects of confounding, also, may not have been adequately controlled."

"The lack of an effect of own smoking on breast cancer risk makes an effect of passive smoking implausible except in regard to childhood exposure, when biological mechanisms may be different. In particular, maternal smoking may be a surrogate measure of in utero exposure, yet we found no effect of maternal exposure on breast cancer risk. It is also relevant that smokers are themselves exposed to the effects of passive smoking."

"In conclusion, we concur with previously published studies of older women with breast cancer in finding no effect of own smoking, alcohol or caffeine consumption on young breast cancer risk. The evidence for a passive smoking effect is weak, and, in view of its biological implausibility, we cannot conclude that there is a causative relationship between passive smoking and breast cancer risk."

Other Health Issues

[1] Bredfeldt, R.C., Cain, S.R., Schutze, G.E., and Holmes, T.M., "Passive Tobacco Smoke Exposure and Bacterial Meningitis," *Clinical Research* 41(4): 754A, 1993 [Issue 80, Item 36]

In this abstract, the authors report that bacterial meningitis, an infection of the membranes around the brain, was statistically significantly associated with household tobacco smoke exposure in a group of 93 Arkansas children aged 2 months to 17 years.

EXCERPTS:

"The purpose of the study was to determine whether there is an association between bacterial meningitis among children and prior exposure to passive tobacco smoke. The case-control design was utilized in the investigation with cases defined as all children admitted with culture confirmed bacterial meningitis to Arkansas Children's Hospital during the period 1989-1992 and an equal number of age and sex matched controls admitted during the same period for abdominal surgery."

"Exposure to tobacco smoke was determined by means of a telephone survey of the primary caregivers. The exposure was classified as 'yes' if there was smoking in the household during the period immediately preceding admission to the hospital. An attempt was also made to quantify the level of smoking in packs per day."

"Survey response rates for cases and controls were 78.6% and 79.6% respectively. Ages of cases ranged from 2 months to 17 years. Approximately 40% were female. Children with bacterial meningitis were more likely to have been exposed to tobacco smoke in the household than controls (Odds ratio = 2.36, 95% CI 1.15, 4.87). In addition to age and sex, the cases and controls were similar with respect to socioeconomic status."

"These findings indicate that bacterial meningitis, in addition to overall respiratory deaths and sudden infant death syndrome, may be related to the effect of exposure to tobacco smoke after birth."

[2] Giebink, G.S., "Preventing Otitis Media," *Annals of Otology, Rhinology and Laryngology* 103: 20-23, 1994 [Issue 80, Item 37]

In this review of the treatment and management of recurrent acute otitis media, the author claims that elimination of parental smoking could be a preventive action that might be taken.

EXCERPTS:

"Recurrent acute otitis media (AOM) is an extremely prevalent disease in young children. Epidemiologic associations suggest that primary prevention or reduction of AOM frequency may be achieved with breast-feeding during infancy, elimination of household tobacco smoking, and use of small rather than large day-care arrangements for infants and toddlers. Secondary antimicrobial prophylaxis with amoxicillin or sulfisoxazole reduces the frequency of recurrent AOM by about 50%, but it does not appear to reduce the duration of otitis media with effusion (OME). Tympanotomy tube insertion is not a effective as amoxicillin in reducing AOM frequency in children without OME. Adenoidectomy appears to be warranted for children who develop recurrent AOM after extrusion of tubes. Vaccines against the common bacteria and viruses causing AOM hold the greatest promise of preventing AOM and blocking the sequence of pathologic events leading to chronic OME and middle ear sequelae. The greatest progress has been made recently with pneumococcal protein conjugate vaccines, and clinical testing is in progress."

"In summary, there are a number of approaches to preventing otitis media. Disease can be reduced with certain primary interventions such as breast-feeding, smoking elimination, and cleft palate identification. In the future, vaccines targeted against otitis media-causing bacteria and viruses will play a major role in disease prevention. Secondary prevention at present consists of antibiotic chemoprophylaxis and, in selected cases, tympanotomy tubes and adenoidectomy.

[3] Kieser, J.A., and Groeneveld, H.T., "Effects of Prenatal Exposure to Tobacco Smoke on Developmental Stability in Children," *Journal of Craniofacial Genetics and Developmental Biology* 14: 43-47, 1994 [Issue 78, Item 32]

The authors of this South African study claim that measurements of dental development suggest that children whose fathers smoked during their mothers' pregnancies, as well as children whose mothers and fathers both smoked during pregnancy, had experienced some level of "developmental stress" while a fetus. However, when additional factors were taken into account, the claimed association disappeared.

EXCERPTS:

"[I]s there evidence for subclinical destabilization of development in children exposed to tobacco smoke from their parents?"

"Given the usefulness of fluctuating odontometric asymmetry as a measure of developmental stress, we decided to compare levels of dental asymmetry in children whose parents smoked with those whose parents did not."

"The possible teratogenic effects of paternal smoking on the unborn has [sic] received little attention. Male smokers have been shown to have significantly fewer and less mobile sperm than nonsmokers. Infants whose fathers smoked also have been shown to have significantly lower birth weights than those whose fathers did not smoke at all. Whether it has a direct effect via the sperm, or an indirect effect via passive smoking of the mother, or both, paternal smoking appeared to have at least some destabilizing effect on the development of our sample. However, it was only when both parents smoked that there was a general and significant increase in the levels of fluctuating asymmetry. The noticeable absence of a gradual increase in asymmetry with increased exposure to tobacco smoke points to the absence of a dose response. Rather, it might be that there is a threshold of response, which is only crossed by significant numbers of children when both parents smoked."

"In contrast to these univariate results stand the multivariate analyses of our results, which showed that in only one out of six comparisons was smoking status a significant predictor of increased asymmetry."

"Our study shows that prenatal exposure to maternal smoking does not result in developmental instability of

the fetus as measured by fluctuating dental asymmetry. Significantly elevated levels of asymmetry were noted only in univariate analyses of children who had suffered in utero exposure to tobacco smoke from both parents. There were no significant differences between the sexes, nor in birth order of the children, nor was there a general multivariate trend towards elevated asymmetry with increased prenatal exposure to tobacco smoke."

[4] **Maw, A.R., and Bawden, R., "Factors Affecting Resolution of Otitis Media with Effusion in Children," *Clinical Otolaryngology* 19: 125-120, 1994 [Issue 79, Item 32]**

A study assessed the therapeutic effect of adenoidectomy and adenotonsillectomy (removal of adenoids and/or tonsils) during a 5-year follow-up in children with a history of otitis media (middle ear infection). The authors report that factors affecting the recurrence of otitis media were whether or not adenoidectomy was performed; the age at the operation; the history of earache prior to surgery; and parental smoking habits.

"There is only limited knowledge of the factors which influence the outcome of otitis media with effusion in children in the long-term. This randomized controlled study assessed the therapeutic effect of adenoidectomy and adenotonsillectomy during a 5-year follow-up. Numerous pre-treatment independent variables concerning the child's upper and lower respiratory tract, atopic status and parental habits were assessed in relation to two dependent outcome measures. These were otoscopic clearance of effusion and no peak/peak tympanometric change."

"A total of 222 children was studied and reviewed annually for 5 years. Four of 43 independent variables were found to be repeatedly significant in relation to outcome: (a) whether or not adenoidectomy was performed; (b) age at operation; (c) history of earache prior to operation; and (d) parental smoking habits. The results provide further evidence of a beneficial effect of adenoid removal and the importance of the age at which surgery is advised. They also suggest the need to investigate further the relationship of superadded acute suppurative otitis media with otalgia and the outcome of chronic otitis media with effusion. Finally, avoidance of parental smoking will have a beneficial effect on children's middle ear disease."

"Treatment for OME, either by myringotomy and VT insertion, or by adenoidectomy is the commonest reason for elective hospital admission for surgery in children."

"Until recently little has been known of the natural history of the untreated condition. Our own studies, however, have shown that in this highly selected group of severe bilateral cases, without any treatment at all, spontaneous resolution of glue occurs in the unoperated ear in the group not treated with either adenoidectomy or adenotonsillectomy in approximately 22% of ears at 1 year, 37% at 2 years, 50% at 3 years, 60% at 4 years, 70% at 5 years, 85% at 7 years and 95% at 10 years. In the early stages of this study we showed that the age of the child at operation had an effect in relation to outcome, both in cases in which the adenoids were removed and in those in which no surgery was carried out. This effect persisted for up to 12 months following intervention. In addition, there was evidence that in the first 3 months following adenoidectomy children with larger adenoids and smaller post-nasal space airways had better outcome than those with smaller adenoids and larger airways."

"The adverse effect of passive smoking on long-term outcome, supports similar data from our own short-term results and form other studies. In this study the deleterious effect of parental smoking is seen to persist for at least 5 years after operation."

"The unexpected finding that the complaint of earache during the 12 months prior to operation has a beneficial effect on outcome was not anticipated and has never previously been reported. . . . Investigation showed that children without earache were not significantly younger, there was no difference in the duration of their hearing loss prior to operation and although they had less discharge than those with earache this was not to a significant degree."

[5] **Poets, C.F., Rudolph, A., Schlaud, M., and Kleemann, W., "Maternal Cigarette Smoking and Sudden Infant Death Syndrome (SIDS) -- Results From the Lower Saxony Perinatal Project," *Pediatric Research* 36: 356, 1994 [Issue 79, Item 33]**

Based on data concerning the number of cigarettes smoked during pregnancy, the authors report that their results confirm previous studies that maternal smoking is one of the most important risk factors for SIDS. ETS is not mentioned.

EXCERPTS:

"Maternal smoking has long been identified as a risk factor for SIDS. However, almost all data available are based on information obtained *after* SIDS had occurred and are, therefore, potentially influenced by recall bias. In Lower Saxony, detailed information concerning the perinatal period, including information on the number of

cigarettes smoked during pregnancy, is routinely obtained for almost all infants born in the region."

"After adjustment for potential confounders (social class, birthweight, maternal age, ethnicity), smoking during pregnancy was still associated with a significantly increased risk of SIDS (odds ratio (OR) 2.7, 95% CI 1.7-4.5)."

"These results confirm previous studies that maternal smoking is one of the most important amongst the potentially amenable risk factors for SIDS."

[6] Stanwell-Smith, R.E., Stuart, J.M., Hughes, A.O., Robinson, P., Griffin, M..B., Cartwright, K., "Smoking, the Environment and Meningococcal Disease: A Case Control Study," *Epidemiology and Infection* 112: 315-328, 1994 [Issue 79, Item 34]

After a rise in the incidence of meningococcal disease in England and Wales, the authors of this study investigated events and exposures immediately preceding the onset of disease. They conclude that the study helped define "environmental cofactors," including the presence of smokers in the home, in the etiology of meningococcal disease.

EXCERPTS:

"There has been an upward trend in both notifications of meningococcal disease (MD) and laboratory isolations of meningococci in England and Wales in recent years: over 5000 cases were notified between 1 January 1988 and 31 December 1992."

"A rise in the incidence of MD in Britain provided the opportunity to investigate possible risk factors in greater detail. Emphasis was placed on events and exposures immediately preceding the onset of disease."

"Apart from information relating directly to MD in cases, the same questions were addressed to cases and controls. Inquiries included: preceding illness, family health history, infant feeding, socio-economic factors, exposures to smoking, alcohol, solvents and dust, leisure activities, the number of people kissed on the cheek and/or mouth (kissing contacts) in the previous 2 weeks, and life events."

"Seventy-four cases were ascertained during the study period: an additional 14 cases, diagnosed clinically but not confirmed, were excluded. Questionnaire interviews were completed for all 74 confirmed cases and for 232 matched controls. Four cases died."

"There was no significant difference between cases and controls in previous history of chronic illness, frequent colds or speech disorders."

"Overall recent drug or medicine consumption in cases was not significantly higher than in controls (OR 1.84, 95% CI 0.96-3.67)."

"There was no association of MD with type of infant feeding."

"Case households tended to have more residents, although this difference was only significant for cases under 5 in households of six or more people. The number of rooms in the households did not differ significantly between cases and controls. However, the mean number of residents per room was higher for cases than for control households."

"The numbers of regular close contacts or of cheek kissing contacts were not associated with illness."

"Fifty-four case households (73%), and 130 control households (59%) reported at least one regular cigarette smoker. This was significantly associated with MD in those aged under 5 years."

"For cases under 5 years, odds ratios rose with increasing numbers of cigarettes smoked daily in the home, and also with the number of smokers in the household. A similar pattern of rising odds ratios for both variables was observed after removal of the confounding effect of social class."

"There was no evidence for an association between MD and the total score for life changes in families of cases and controls over the previous 6 months. . . . Nevertheless, certain life events were significantly more common in cases and their families than in those of controls."

"Forty-five cases (61%) had been exposed to dust within 2 weeks of onset. . . . Of the six different types of dust specified on the questionnaire, only plaster, brick or stone dust exposure was significantly associated with acquiring MD. . . . There was no evidence of an association with exposure to chemicals, including six commonly used types of solvent."

"[D]ampness was not reported more frequently by interviewees in homes of cases and there was no significant difference between the instrumental measurement of dampness of homes of cases and controls."

"There was no evidence of an association between MD and leisure activities, including contact with pets, physical exercise or recently increased physical activity, sports and visits to public places, swimming pools, religious ceremo-

nies, parties or clubs. Visits to smoky places in the preceding 2 weeks were not associated with meningococcal infection. Alcohol consumption, including gripe water in infants, was not significantly increased in cases."

"This study has helped to define environmental co-factors in the aetiology of MD. In the associations between passive smoking, overcrowding, bed sharing, mouth kissing and nights away from home, the common factor is the likelihood of greater exposure to meningococci. Cigarette smoke and dust may enhance invasion via the nasopharynx; stressful life events also appear to increase susceptibility."

[7] **Willinger, M., Hoffman, H.J., and Hartford, R.B., "Infant Sleep Position and Risk for Sudden Infant Death Syndrome: Report of Meeting Held January 13 and 14, 1994, National Institutes of Health, Bethesda, MD,"** *Pediatrics* **93(5): 814-819, 1994 [Issue 77, Item 39]**

Based on a review of data on SIDS and infant sleeping position from around the world, a meeting of experts recently concluded that a change to back or side sleeping position (as opposed to prone) was associated with a reduction in SIDS rates. It was noted that, in the countries for which data were examined, parental smoking rates had not changed, nor had breast-feeding rates.

EXCERPTS:

"The rate of SIDS in the United States has remained relatively unchanged despite significant declines in total infant mortality in the past decade. This was the experience for most of the developed world up to the past few years. Now several countries that are promoting side or back sleeping for infants are reporting significant declines in the incidence of SIDS. This article summarizes the deliberations of an international conference that was convened to critically evaluate the role of prone sleeping in SIDS."

"On January 13 and 14, 1994, NICHD [National Institute of Child Helath and Human Development], with co-sponsorship from NIDCD [National Institute on Deafness and Other Communication Disorders] and NCHS [National Center for Health Statistics], Centers for Disease Control and Prevention (CDC), convened a second international scientific meeting, with observers from concerned organizations to: (1) review information regarding trends in infant mortality and the effects of public health interventions overseas to prevent SIDS, (2) review preliminary data on SIDS and prone sleep position in the United States and (3) discuss how the information could be used to guide further activities in the United States."

"In New Zealand, Tasmania, and Avon, which have the longest experience with >80% back or side sleeping, the SIDS rates have remained low for 2 or 3 years. No significant changes were observed in other parental behaviors targeted by the risk reduction campaigns, such as cigarette smoking or breast feeding. Therefore, the reduction in SIDS rates presumably has resulted from a change in infant sleep position."

"After discussion, the overwhelming opinion of the panel and assembled experts that the evidence justified increased effort to reach a greater diversity of health care professionals, parents, and other caregivers with this information. Strategies to eliminate or control the environmental factors that may be mediating prone position risk, such as infection and the use of soft bedding under the infant, were considered important but not sufficient. Infants with contraindications such as those with craniofacial abnormalities and gastroesophaegeal reflux should still be placed prone for sleep. The premature infant was also discussed, with no resolution. In Norway, Australia, New Zealand, and Britain, the premature infant, who is asymptomatic at discharge, is placed to sleep nonprone."

"The panel concluded that the following actions should be encouraged: (1) The NICHD/NIH continue to study and monitor prospectively the impact of public health initiatives on infant health and provider practices, and promote research to understand the causes and mechanisms of SIDS; (2) the AAP [American Academy of Pediatrics] and other professional organizations increase their efforts to educate practitioners and advise parents regarding the existing AAP recommendation; (3) federal agencies support the professional and parent communities with parallel initiatives."

ETS EXPOSURE AND MONITORING

[1] **Carmichael, P.L., Hewer, A., Jacob, J., Grimmer, G., and Phillips, D.H., "Comparison of Total DNA Adduct Levels Induced in Mouse Tissues and Human Skin by Mainstream and Sidestream Cigarette Smoke Condensates." In:** ***Postlabelling Methods for Detection of DNA Adducts.*** **D.H. Phillips, M. Castegnaro, and H. Bartsch (eds.). Lyon, International Agency for Research on Cancer, 321-326, 1993 [Issue 76, Item 39]**

Based on in vivo and in vitro tests of mainstream and sidestream smoke condensates, the authors claim that